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VESICOVAGINAL FISTULA*
AN APPRECIATION OF MARION SIMS AND HIS WORK

DOUGAL BISSELL, M.D., F.A.C.S.

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THE compliment paid me when I was invited to give this address I recognize to have been, in reality, paid to the Woman's Hospital in the State of New York, and as an introduction, may I be permitted to recall briefly the dramatic origin of this institution, which is today a living and growing monument to its founders, Sims and Emmet.

From the Southland of the States to the Metropolis of the nation there came, in 1854, the surgeon J. Marion Sims, in search of health. His theoretical education and practical training in the art and science of medicine had been only that acquired by the average American student of his day. Although poorly equipped, he possessed mechanical ability, imagination, good judgment and an ardent desire to serve humanity. The great lesson taught him by the hardships of the wilderness was self-reliance; with this, together with ingenuity and the love of scientific adventure, he met his daily problems. In the district from which he came he had been a pioneer and leader in the field of surgery, but the Metropolis knew him not. In his great struggle for recognition in New York he showed not only the spirit of youthful enthusiasm, but a rare knowledge and skill in surgery, acquired by his experience in the backwoods of Alabama. Single-handed he fought to arouse interest in the operation he devised for the cure of vesicovaginal fistula, but professional jealousy overwhelmed him, and his efforts seemed doomed to failure, when the timely sympathy and aid of a few farsighted, noble women of influence and means came to his rescue.

In a small private dwelling, during the year 1855, the Woman's Hospital was launched upon its career. The profession objected to its existence on the ground that the field of work in which it proposed to engage, viz., destructive injuries of the vesicovaginal septum, was too limited to warrant an institution for their special care and treatment. Sims' experience, however, had awakened him to the realization of the fact that throughout the land there had existed, for many years, an accumulated number of women made derelicts by this tragedy of childbirth, and to the still more important fact that the surgical staff of no institution, then existing in New York, was capable of relieving a single victim of vesicovaginal fistula. The element of particular interest here is that the "Woman's Hospital" was organized solely for the purpose of curing vesicovaginal fistula, and the justification of its founding soon became apparent for, as its

* Read before the Royal Medical Society of London, Eng., Oct. 19, 1928.

reputation kept pace with Sims' and Emmet's remarkable operative achievements, it outgrew its capacity and expanded into an imposing structure, to be known whereever surgery was known.

That you may better visualize the sufferings of those whom Sims sought to relieve, permit me to relate briefly the story of Mary Smith, the first patient upon whom Sims operated at the Woman's Hospital. She had but recently arrived in America, as an immigrant from the Western coast of Ireland, a pitiable, ill-smelling, repulsive creature, with an extensively excoriated vulva, the result of a continued escape of urine. When the anterior vaginal wall was exposed, a greyish mass came into view, projecting well into the vagina. It appeared to be a very large stone, but, on examination after its removal, it proved to be a wooden float from a seine, about the size of a goose egg; this had been introduced into the bladder, through a large vesicovaginal opening, by her medical attendant at home, to support the superior surface of the bladder, and to prevent it from protruding through the fistulous opening, forming, with the intestines, a true vesical hernia. The float was, of course, completely encrusted with phosphatic deposits, and its removal was thereby rendered difficult, and, to the patient, extremely painful. Most of the base of the bladder and of the urethra was destroyed, but, through the combined efforts of Sims and Emmet, these tissues were reconstructed and restored to function, and for six years or more this woman was employed as a helper in the Hospital.

During the first year of the Hospital's existence, its surgical records were kept with indifference. This failure, however, soon became apparent to Emmet, who possessed hospital training, and to him is due the credit for their eventual accuracy and for the invaluable information which may be garnered from them today. When reviewing these statistics from a numerical standpoint, it should be remembered that before the work on vesicovaginal fistula was systematically begun, it was generally considered too restricted for special consideration; also that the Hospital was closed during three months of the year, for a reason then thought valid, viz., that wounds did not heal well in Summer.

Emmet states that during his early career as surgeon to the Woman's Hospital, 1856–1861, he operated for the repair of vesicovaginal and urethrovaginal fistulae, on an average of twice a week. But a better idea of the actual number of cases which came under his care is obtained through his report at a later date, 1867, analysing 275 cases of injuries to the vesicovaginal septum.*

In reviewing the statistics of the Woman's Hospital during the past ten years (the Hospital being open throughout the entire year, and eighteen surgeons operating), we find that only 58 patients have been operated upon for the repair of vesicovaginal and urethrovaginal injuries. The question naturally arises, Why this great difference in the number of patients suffering from this condition, namely, 275 under the care of one surgeon, the Hospital being open only nine months of the year during approximately ten successive years; and 58 patients under the care of eighteen surgeons, the Hospital being open throughout the entire year during approximately the same length of time? The answer seems apparent, viz., improvement in obstetrical management, and the division of material among a great number of surgeons. It would, however, be erroneous to conclude that, because the art and science of obstetrics has greatly advanced since Sims' and Emmet's time, the vesicovaginal fistula will soon be a thing of the past. The poorly equipped professional attendant and the attendant who has no scientific training constitute, in reality, a large proportion of the workers in the field of obstetrics and,

* Emmet, on another occasion, reported 171 cases, and Sims, eight years after his initial success, reported a series of 261 cases of vesicovaginal and rectovaginal fistulae, of which number 216 were permanently cured; of the remainder, 36 he considered curable, and 9 incurable.

like the poor, will be with us always; but even under the guidance of trained and competent attendants vesicovaginal injuries occasionally occur. It is therefore reasonable to conclude that vesicovaginal fistulae, arising from obstetric causes, will remain with us to tax the ingenuity of the surgeon for generations yet to come. However, while obstetrics will always be the chief aetiological source of vesicovaginal fistulae, gynecological surgery upon the pelvic organs of the female will rank next in importance.

What was the status of the vesicovaginal fistula operation in America, prior to the advent of Marion Sims? The malady had occasionally been cured, but the successes had been spasmodic, and no surgical effort had yielded a definite plan that could be followed with reasonable hope of success. Of the early American surgeons, George Hayward, of Boston, Massachusetts, contributed perhaps more towards establishing a technique for the closure of vesicovaginal fistula than had any of his contemporaries. His position, as surgeon to the Massachusetts General Hospital, brought him in daily contact with advanced medical thought throughout the world, and assured him extensive surgical opportunity; yet in speaking of vesicovaginal fistula and the efforts which had been made to cure it, we find him saying: "It is by no means settled what is the best mode of treating this distressing infirmity." This discouraging attitude, however, was not confined to America, for Henry Earl, in 1829, stated that "under the most favorable circumstances, these cases present the greatest obstacle, and are certainly the most difficult that occur in surgery." Hayward began his work on the repair of vesicovaginal fistulae in 1839 and continued to be actively interested in it until 1851. During this period he operated twenty times on nine patients, with only three successes. Hayward operated in the lithotomy position, and access to the fistula was gained by lateral wooden retractors; further to facilitate approach, he passed a rubber bougie through the urethra to the base of the bladder near the fistula, and, by raising the handle of the bougie, he forced the fistula towards the vaginal outlet and into view. With regard to preparing the orifice, he suggested that, to avoid injury to the bladder, "the membrane of the vagina be dissected up to a considerable extent around the orifice, and that the needle be carried through this at some distance from the edge of the wound." Hayward's object, it would seem, in separating the bladder and vaginal walls in a limited way, was to produce a broader surface for apposition. I interpret his description of the passing of the needle to mean that the sutures should be placed well beyond the angle formed by the separation of the two structures, so that, when the sutures were tied, the separated surfaces would be forced apart and the broadest surfaces made to appose. But, judging from his poor results, his theory did not prove practical. The probability is that some of the sutures penetrated the separated surfaces, occasioned irregularity in apposition and prevented a wide contact, thus encouraging seepage with failure of union. Hayward used dental silk, which offered several objections. Under tension, silk cuts tissue, and its capillary action, in a field surgically unclean, encourages infection of the wound. Hayward candidly admitted that his technique could not be applied where great loss of tissue had occurred. It would seem, therefore, fair to conclude that although Hayward antedated Sims, by thirteen years, in the surgical feat of curing vesicovaginal fistula, he failed to develop a technique which yielded satisfactory results or could be applied to any form of fistula but the very simple. Hayward may be awarded priority in separating the vaginal wall from the bladder, but as his purpose in doing so was not to unite these layers separately, he cannot be considered the originator of the bladder mobilization or flap-splitting technique of today.

The next important effort by an Ameri-

can surgeon was that of Dr. Mettauer, 1847, and the feature of particular interest in his technique is the use of lead sutures.*

Before Sims' successful work, European surgeons had taken but little interest in the cure of this disease.† Lillemand, of France, 1825, records perhaps the first cure. This was done by the combined use of nitrate of silver and approximation of the cauterized edges of the fistula by a form of stilette passed through the bladder wall. Of the 15 cases treated, he reported 4 cures. This technique was applicable only to very small fistulae.

Hayward thought that Dieffenbach's technique was dangerous, because it permitted of the penetration of the bladder. It is evident that Dieffenbach's successes were few.

M. Jobert introduced his plastic method previous to Sims' initial work. The success he obtained was limited, and among the objections offered to it is this: that the transplanted flap, which was usually taken from the large labia, may, and on one occasion did, continue to produce its growth of hair.

In 1834, Gosset of London used a metal suture in the form of gilt wire. There seems to have been much in common in the methods of Gosset and Sims, for the former used, not only the metal suture, but a perineal retractor, and also operated in the knee-chest position. Although his results were seemingly far better than those of his contemporaries in this field of work, his technique did not gain wide recognition, was not generally accepted and therefore was not perpetuated.

These were the principal vesicovaginal fistula techniques before that of Sims was given to the world in 1852, and it will be seen that some of them have features in common with and bearing a close relationship to his.

The method which I was taught by Emmet as being that of Sims differs considerably from that described by Sims in his early work. Even the interesting illustrations in Henry Savage's "Female Pelvic Organs" vary from his original plan. The essential differences between his original plan and that which eventually became recognized as his, and by which the operations herein described were carried out, are as follows: In the former the knee-chest position was used, and in the latter, the semi-prone or Sims' position. In the former a short, imperfect speculum was used; in the latter, an improved speculum which now bears his name. In the former, the denudation about the fistula was made at a right angle to the general direction of the vagina, and did not extend much beyond the vaginal limits of the orifice; in the latter, the denudation was made, whenever possible, in the general direction of the vagina, elongated and greatly widened. In the former he used a long, awl-shaped, spear-pointed needle; in the latter, a short, slightly curved, ordinary surgical needle, with a carrying thread to which silver wire was attached. In the former he used what he called the "clamp or quill" suture; in the latter, the simple twisting of the wire over the line of approximated surfaces, the points of the wire being protected by perforated and crushed shot. I am of the opinion that several of these changes were, in part at least, due to Emmet's influence.

The technique used in the cases herein reported was, in brief, as follows: The patient was placed in the semi-prone or Sims' position, with Sims' speculum retracting the perineum.* The denudation of the vaginal mucosa was made broad, whenever possible, and in the general direction of the vagina. The silver wire

* Mettauer used lead sutures in 2 of the 6 cases reported by him. One of these was successful, and 1, after eight attempts, was a failure. The remaining 4, it would appear from his report, were unsatisfactory.

† To Simon credit should be given for the development in Europe, to the point of success, of the operation for vesicovaginal fistula. This was done independently of Sims' work, although immediately following it. It proved practical in extensive lesions, and sufficiently simple to be learned and followed by his colleagues.

* Neither the Sims position nor speculum was used in Case VI.

suture was attached to a carrying thread which, in turn, was tied to the needle in such a manner as to produce a knot smaller than the heel of the needle; the silver wires were twisted over the line of approximation of the denuded surfaces, and the free ends of the wires were protected by perforated, crushed shot.

The features to be emphasized in the Sims' technique are the following: The denudation surrounding the vaginal orifice of the fistula should be broad and elliptical down to the immediate region of the bladder mucosa, but never involving it. The needle should penetrate, deeply, the vesicovaginal septum, but never involve the bladder mucosa. The wire loop, by which the wire is attached to the carrying thread, should be crushed, so as to occasion the least possible resistance on being pulled through the tissues.

I present for consideration, and as the basis for discussion, 6 cases, 4 of which are vesicovaginal, 1 vesico-urethro-vaginal and 1 uretero-vesico-vaginal. All of these cases involve the vesicovaginal septum, and are selected from a considerable number that have come under my care during the past thirty-seven years, because they are unusual in type or in origin, and serve to demonstrate the value of Sims' technique in complicated conditions. It seemed preferable, in preparing this study, to concentrate upon a few selected cases, rather than to report a greater number of simple character which might be cured by any of the varied techniques now in vogue. It is the complicated and unusual type which the surgeon of today finds difficult, and for the cure of which he does not always have a method at his command.

My position in this discussion is that the principle in the technique first formulated by Sims is more nearly uniformly applicable to the varied forms of vesicovaginal and urethrovaginal fistulae than any technique used before or since his day. The following histories are condensed, and include only such material as bears directly upon the discussion:

Case 1. Vesicovaginal fistula complicated by occlusion of the urethra at its vesical orifice. During a vaginal hysterectomy performed

Fig. 1. Case 1. Before operation. Showing urethral obstruction and fistula.

one year previous to this patient's admission to the Woman's Hospital, the bladder was injured and a vesicovaginal fistula resulted. Later an unsuccessful effort was made, by the same operator, to close the fistula. This attempt not only was a failure, but terminated in extensive local deformity and severe interval pain in the lumbar region, occasionally associated with vomiting. A description of the method which had been adopted to close the fistula could not be obtained. Vaginal examination showed a short vaginal tube with dense scar tissue, and a large vesicovaginal fistula at the vault. Urethral examination showed a complete obstruction of this organ at the vesical neck. The first problem for consideration, therefore, was restoration of the urethral neck.

Operation 1, for restoring the urethra (Oct. 18, 1923). Through a transverse suprapubic incision, the bladder was partly detached from the pubic bone. A median longitudinal incision was then made through the bladder wall, down to within a short distance of the vesical neck. The vesical opening into the urethra was found to be completely obliterated; there was not even a depression at this point. The base of the bladder was greatly

deformed, as the result of scar tissue which began at the area of the neck and terminated at the area of the vaginal vault, where an

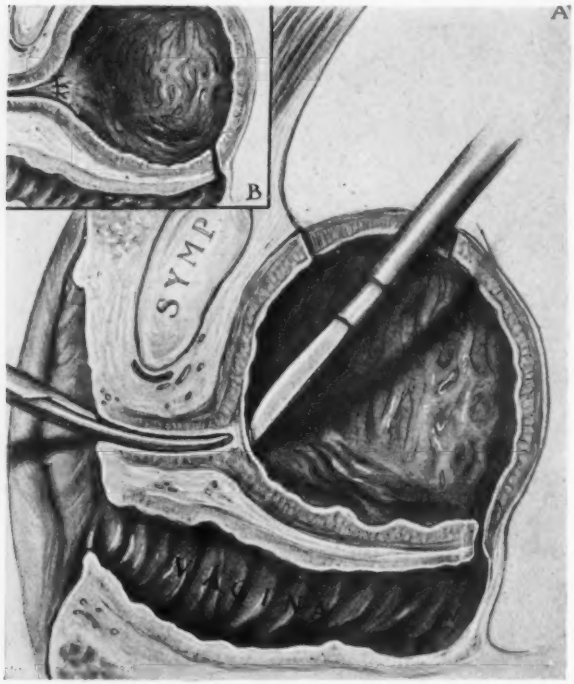

Fig. 2. Case 1. (A) Urethral barrier being incised. (B) Canal made patent.

opening into the vagina was found. The left ureteral orifice could not be determined. A curved forceps was then passed through the urethra, from without to the area of occlusion at the neck of the bladder. Its blades were opened and an incision made between them, through the bladder wall into the urethral canal. The forceps were then withdrawn, and the mucosa of the bladder was stitched to that of the urethra with interrupted No. 0 catgut sutures. Convalescence was uninterrupted. The reconstruction of the canal was satisfactory, but, as there seemed to be a tendency of the newly formed orifice to contract, dilating of the canal at intervals was necessitated.

Operation 2, for closure of the vesicovaginal fistula (Jan. 24, 1924). The vesicovaginal fistula located at the vault of the vagina was successfully closed by Sims' technique, eight silver wires being used and Sims' catheter inserted. Since then, now nearly four years, the bladder has been functioning normally, but the interval pains in the left lumbar region continue.

Result: Satisfactory.

COMMENT

The particular interest in Case 1 is the extent of injury done to the neck and base of the bladder. Not only was the vesical opening leading into the urethra completely obliterated, but the injury along the base of the bladder so involved the left ureter as to hide its orifice, and, judging from the persistency of the interval pain, partly to obstruct the canal. The sequelae following the first effort made to cure the vesicovaginal fistula were, therefore, three distinct lesions; complete obstruction of the urethra, partial obstruction of the left ureter, and a vesicovaginal fistula at the vaginal vault. The vesicovaginal fistula at the vault of the vagina was surrounded by dense scar tissue, with the vaginal wall and bladder anterior, and the vaginal wall and peritoneum posterior. It might fairly be said, in regard to the closure of the vesicovaginal fistula, that, in view of the amount of scar tissue at the base of the bladder involving urethra, ureter and vaginal vault, any method which called for the separation of the bladder from the vaginal wall would, under these circumstances, have been not only difficult, but dangerous to apply, and, if by chance successful, could not have accomplished more than did the method adopted.

Case 11. Uretero-vesico-vaginal fistula with both ureteral orifices exposed vaginally.*

An abdominal hysterectomy was performed by me upon this patient at the Woman's Hospital, January 1912, because of an extensive carcinoma of the cervix. The malignant growth extended from the right side of the cervix, well into the pelvis, retroperitoneally. The pathologist's comment was: "This gross specimen is one of the largest cervical cancers I have ever seen successfully removed." The growth completely surrounded the right ureter at the base of the broad ligament, and measured 5 cm. in length and 4 cm. in diameter. The uterus, its adnexae, the growth and more than 5 cm. of right ureter were removed. In so doing, it was found necessary to remove a

*Reported in the *Bulletin of the Woman's Hospital*, Oct., 1913.

considerable portion of the base and posterior wall of the bladder; the free end of the right ureter was anchored, under considerable tension, to the right angle of the bladder opening, and vaginal drainage was established. The patient made an uninterrupted recovery, but the bladder wound opened completely at the vault of the vagina. Vaginal examination showed a large vesico-vaginal fistula crossing the vaginal vault from the implanted ureteral orifice on the right side to the normal ureteral orifice on the left side. The orifices of both ureters were distinctly seen per vaginam.

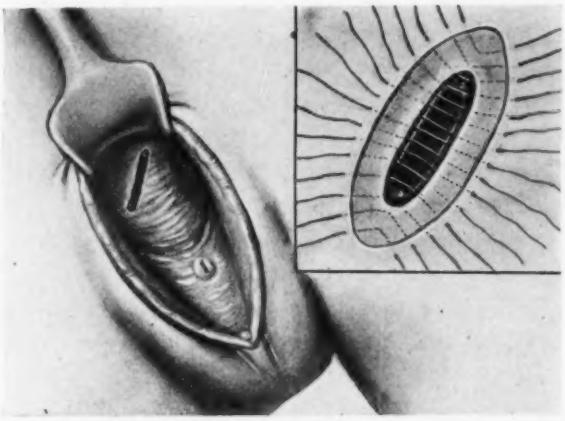

Fig. 3. Case 2. Both ureteral orifices exposed vaginally. (Insert) Repair of fistula with fifteen silver wire sutures.

Operation for closure of the vesicovaginal fistula (Jan. 25, 1912). Six weeks after the operation above described, the edges of the fistula appeared healthy, and repair by the Sims method was made. Because of the exposed ureteral orifices, denudation of the vaginal surfaces about the fistula was done with great care, so as not to encroach upon the ureteral orifices. Fifteen silver wire sutures were required to ensure proper apposition. Their placement had to be so manipulated as to invert the ureteral orifices into the bladder yet not constrict them. The wires were removed at the end of two weeks. Primary union resulted. The entire operative field remained healthy until her death, which followed the primary operation in about six months, as the result of metastatic developments in the upper abdomen.

Result: Satisfactory.

COMMENT

This is the largest vesicovaginal fistula which I have ever closed or seen closed. Further, it is the only case I have operated upon where both ureteral orifices could be seen per vaginam. It is of interest also from the fact that the initial operation so radically eliminated the cervical cancer, which had extensively involved adjacent tissues, that in six week's time repair was made in a tissue which showed no evidence of preoperative pathology. No other technique could have accomplished more, in this case, than did Sims' and I think that the success of the application of any other would have been extremely doubtful.

Fig. 4. Case 3. Catheter in left ureter. Demonstrating close proximity of fistulous opening to ureter.

Case III. Vesicovaginal fistula formerly vesicoabdominal fistula.

Following the second labor of this patient, pelvic infection occurred, culminating in an abscess at the base of each broad ligament. One abscess ruptured in the region of Poupart's ligament on the left side, and the other ruptured in the same region on the right side. From the left side, pus and urine escaped; from the right side only pus escaped. The right side closed spontaneously, but the left continued to discharge pus and urine. At the end of three months a puncture was made at the base of this abscess cavity to drain it into the vagina. The opening over Poupart's ligament then closed, but leakage of urine into the vagina became continuous. This

patient came under my care one year after the initial lesion. Vaginal examination in Sims' position showed an opening on the

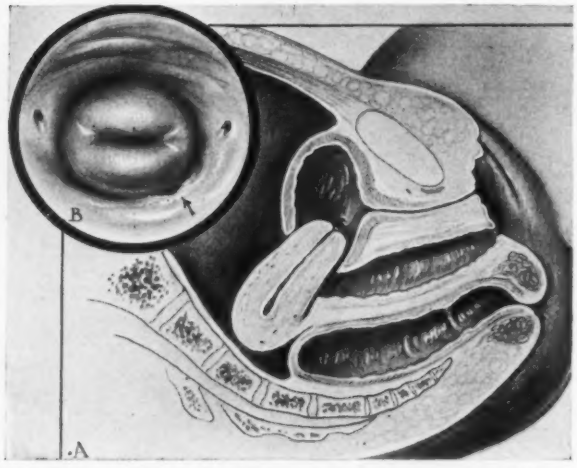

Fig. 5. Case 4. Cervix of retroverted uterus in bladder cavity. Vesicovaginal fistula following posterior wall of cervix.

anterior vaginal wall, 2½ cm. from the cervix and to the left of the median line. A cystoscopic examination was made after plugging the opening on the vaginal side, and a slit at the base of the bladder, 1 cm. in length, was seen in close proximity to the left ureter.

Operation for closure of the vesicovaginal fistula (April 22, 1926). Immediately before the operation to close the fistula, a catheter was passed into the left ureter, to remain as a guide throughout the operation. In order to bring the field closer to the introitus, a catgut suture was passed through the anterior lip of the cervix, then through the tissues of the posterior fornix. On tying this suture the cervix was forced well back out of view, the anterior wall put on greater tension and brought closer to the operator. A wide and long denudation was made on each side of the fistulous opening, in the direction of the long axis of the vagina. Eight silver wire sutures were inserted to approximate the denuded surfaces. Throughout the operation, the ureteral catheter was moved up and down, to determine whether or not the stitches included the ureter. A cystoscopic examination was made immediately after the operation. No suture could be seen exposed on the vesical surface; no leakage discovered on distending the bladder. Sims' block-tin catheter was inserted.

Result: Satisfactory.

COMMENT

This case presented no special difficulty in regard to the closure of the fistula, excepting that care had to be taken, because of the proximity of the fistula to the ureter, not to include the ureter in the stitches. It is difficult to say whether the original injury was ureteral or vesical, but when an abscess occurs at the base of the broad ligament the ureter is always endangered.* It is possible, therefore, that the original injury was to the ureter and, when the blind puncture was made at the base of the abscess cavity, the bladder wall was punctured. The ureteral injury then closed and the vesical injury remained.†

Case iv. Vesicovaginal fistula with cervix in the bladder.

Ten years before this patient's admission to the Woman's Hospital she was delivered normally of a full term child. Soon after delivery incontinence of urine occurred and was continuous. Menstruation regular and without pain; amount of flow moderate.

Bimanual examination showed a very considerable shortening of the vaginal tube, and narrowing at the vault; the cervix could not be felt; a body could be clearly outlined, fixed in the pouch of Douglas. Vaginal examination in Sims' position, and with the assistance of a speculum, showed an opening on the anterior vaginal wall, about 2 cm. from the vault and to the left of the median line; through this opening urine was seen to escape. Another opening was discovered near the vault, through which the probe passed posteriorly to the depth of 2 cm. The cervix could not be located. There was a considerable amount of scar tissue in the vaginal vault. Cystoscopic examination showed the cervix to be located in the bladder, between and a little anterior to the ureteral orifices. The opening of the fistula was seen anterior to the cervix and a little to the left of the median line.

* An illustrative case may be found in *Am. J. Obst. & Gynec.*, 47: 145, 1903. (Bissell.)

† Sims performed several hundred operations for the repair of vesicovaginal fistulae before he lost a case by death. This death occurred with the first patient upon whom he operated in England in the early 'sixties, and the autopsy showed that the ureters were encircled by the stitches. As far as I am able to discover, this is the only accident of the kind which he had.

Operation 1. For the removal of the corpus uteri and freeing of adhesions (Aug. 13, 1926). It was deemed advisable to perform abdominal amputation of the corpus uteri before attempting to close the fistula. The abdomen was therefore opened and the retroverted, fixed corpus freed and removed; also, the right ovary was resected because of an hemorrhagic cyst, and the omentum, firmly adherent to the anterior surface of the uterus and to the broad ligaments, was freed.

Operation 2. For closure of the vesicovaginal fistula (Aug. 27, 1926). Four weeks after the removal of the corpus uteri the vesicovaginal fistula was closed by the Sims' method. Seven silver wire sutures were used. Sims' block-tin catheter was inserted.

Result: Satisfactory.

COMMENT

When we remember that, in an extreme degree of retroversion, the cervix assumes an extreme anterior position in close apposition to the anterior wall, it is easy to understand how, when a large opening exists in the vesicovaginal septum following labor, and the uterus retroverts, the cervix will slip through the opening into the bladder; and, when the injury partly heals, a fistula will form along the wall of the anteverted cervix. In the early days of gynecology such cases were more often seen than they are now. This is comprehensible when we recall the fact that vaginal injuries were then common and extensive, and also that, as the result of poor obstetrics, retroversion of the uterus following labor occurred more frequently.

It is my opinion that in this case the flap-splitting method in vogue today would have been difficult, if not impossible to apply and, if adopted, could not have given better results.

This case was operated upon by Dr. Albert H. Aldridge, one of the junior surgeons at the Woman's Hospital, and I include it in this report not only because of its present-day rarity, but because I was in counsel with Dr. Aldridge throughout the operations, and am therefore indirectly responsible for the results. The application of any technique would here have been difficult. Success was the result of skill and exactness in the execution of the technique employed. The reasons for the removal of the corpus uteri were to avoid possible extension of infection from the bladder, if such occurred, to remove a definite pelvic pathology, and to prevent the menstrual flow, or any other uterine flow, from passing into the bladder.

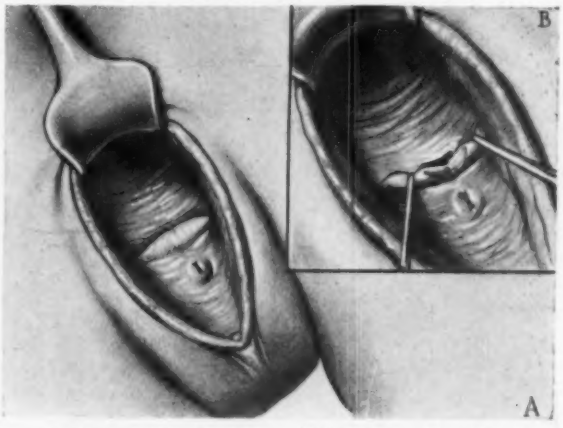

Fig. 6. Case 5. Destruction of bladder wall at its junction with urethra, with bridge of scar tissue.

Case v. Vesico-vaginal fistula with complete destruction of the neck of the bladder complicated by an embedded broken needle.

This patient was delivered instrumentally five months before entering the Woman's Hospital. Since delivery there was a continuous escape of urine. Examination showed that the vesicovaginal septum, at the junction of the bladder and urethra, was completely severed transversely. It appeared as if the triangular ligament area below the pubic arch had been torn away from its moorings, leaving a large opening at the neck of the bladder, through which a finger could be passed into the bladder or urethra. The urethral portion of the wound, on healing, formed a dense scar which extended to each ramus of the pubes, behind which the fistula, in greater part, was hidden. The tissue in the angles of the wound consisted of scar tissue and periosteum.

Operation 1, for closure of the vesicovaginal fistula (July 2, 1926). In order to facilitate vision of and approach to the fistula, the perineum was incised medianly down to the sphincter, and the dense scar tissue at the base of the urethra was severed in the direction of the axis of the vagina. These procedures

not only permitted good exposure but facilitated denudation of the edges of the fistula. Sims' technique was then applied transversely

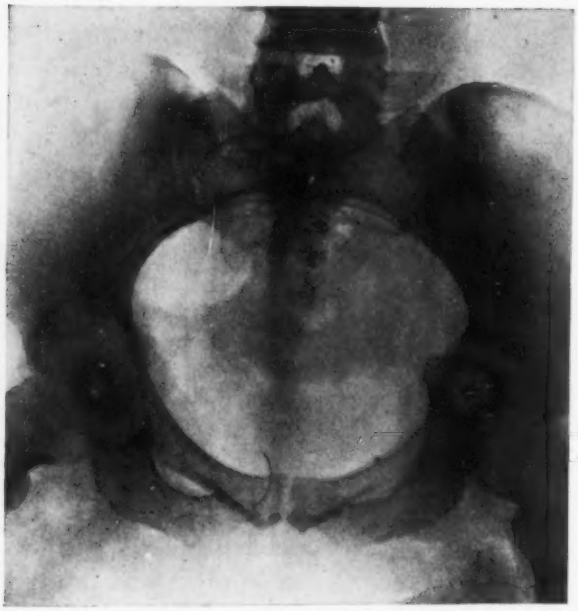

Fig. 7. Case 5. Roentgenogram showing broken needle imbedded in tissues under the pubic area.

to the axis of the vagina, eight silver wire sutures being used to approximate the denuded surfaces. Great difficulty was experienced in passing the needles through the tissue in the region of the rami of the pubes, and, because of the unyielding character of the tissue, a needle broke. As the portion of the broken needle seemed completely buried in the tissue, it was deemed advisable not to attempt to remove it then, fearing that so doing might result in greater injury to the vesical structures, and hoping, also, that the needle might become encysted and not interfere with primary union. The Sims block-tin catheter was not inserted in this case, fearing that, as the catheter would rest on the line of sutures, the tissue between might be pressed upon to the extent of endangering union. The mushroom catheter was not used because it was feared that the resistance, on removal from time to time, would disturb the apposition of the tissues at the neck of the bladder. Eight days after the operation leakage occurred. The stitches were soon removed and a small opening was found. A roentgen-ray picture was secured which showed the needle to be in the immediate area of the opening.

Operation 2, for removal of needle and closure of remaining small fistula (Aug. 20, 1926). On passing a small probe through the opening, it came in contact with the needle partly exposed in the bladder. A small artery

Fig. 8. Case 5. Roentgenogram showing silver wire in position, twelve days after removal of needle.

clamp was then passed through the opening, the needle grasped, counter pressure made on the anterior wall of the vagina, the point of the needle forced through into the vagina, and the needle removed. This manipulation necessarily dilated, somewhat, the fistula. The tissues about the opening were freely denuded in the direction of the axis of the vagina, and five silver wire sutures were used. Sims' block-tin catheter was inserted.

Result: Satisfactory.

COMMENT

There is little to be said in comment on this case. I might be criticized, with some justice, for not having proceeded, at the time of the initial operation, to remove the broken needle. The difficulties encountered and, as I saw them, the possibilities of causing greater injury by an effort to secure the needle, seemed to me prohibitive of the attempt. This case stands out in my mind as one in which neither the flap-splitting technique nor the transplanting of adjacent tissues was applicable.

Case VI. Urethrovaginal and vesicovaginal fistula.

Two years before this patient's admission to the Woman's Hospital, the vaginal outlet had been severely injured about the neck of the bladder and urethra, during a difficult instrumental delivery. Previous to her admission, four surgical attempts to close the large vesical opening were made but without success. Examination on admission showed that the urethra and neck of the bladder had been completely torn away from the right ramus and pubic arch and displaced to the left. A large opening existed where the neck of the bladder and base of the urethra were previously located. There existed also another opening through the right lateral wall of the urethra. These openings were in close proximity and their directions were at a right angle to each other. The tissue of the vulva, to the right of the vesical fistula, showed several scars which resulted from previous unsuccessful operative efforts made to close the vesical opening, by removing strips from the labia and transposing them to the denuded edges of the vesical opening. Immediately under the pubic arch there remained but little tissue save scar and periostium.

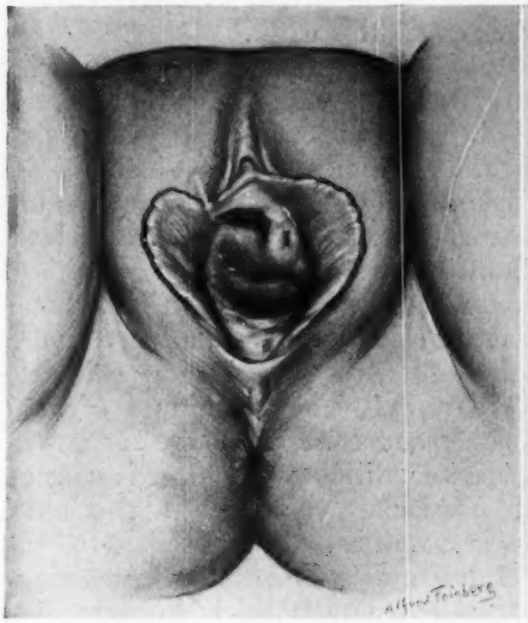

Fig. 9. Case 6. Urethrovaginal and vesicovaginal fistulae before operation.

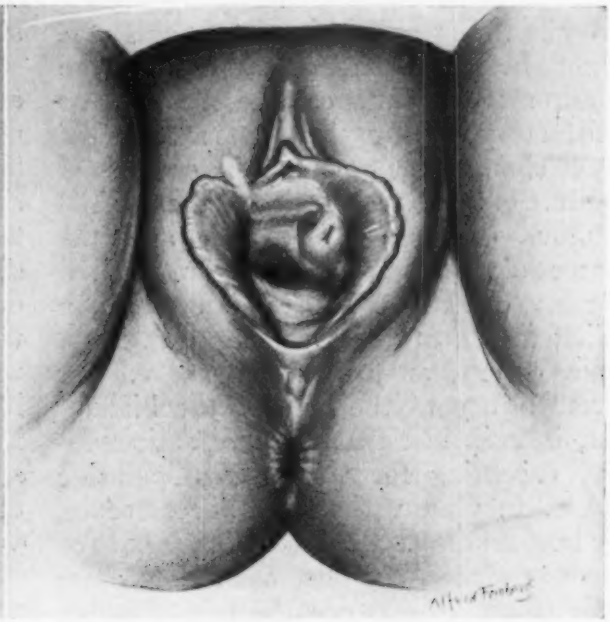

Fig. 10. Case 6. Vesicovaginal fistula repaired. Urethrovaginal fistula to be repaired.

Operation for closure of the vesico-vaginal fistula (Sept. 14, 1927). The denudation about the fistula, particularly under the pubic arch, was rendered difficult because of the extensive loss of normal tissue; and also, the passing of the needles was made difficult on account of the unyielding character of this tissue. Three needles were broken during the operation, but all were easily removed. This necessitated repassing of the needles, which greatly weakened the tissue below the pubic arch. Seven silver wire sutures were used in closing the fistula. It was deemed unwise to attempt to close the urethral fistula at the same sitting. Sims' block-tin catheter was inserted. On removing the stitches the result seemed satisfactory. Four days after the removal of the sutures the patient complained of a slight moisture at the vulva. Examination did not reveal an opening but, on injecting the bladder with an argyrol solution, oozing could be detected between the line of union and the pubic arch, but from an opening too small to be clearly defined. Its location being above the line of union convinced me that it was a stitch opening, the result of injury to the thin tissue by the repeated passing of the needles. The patient was then kept in bed for ten days, with a catheter in position. At the end of that time, there being no perceptible leakage, she was discharged in a satisfactory condition. I have had no opportunity since then to see the patient, as she lives in an adjoining State and cannot afford to visit me, but,

according to a communication from her attending physician, she is doing well.*

COMMENT

While the mechanical result in this case might be called in question, yet the symptomatic results can be recorded as satisfactory to the patient. The mechanical result should not, however, be considered a failure of Sims' technique, for the original fistulous opening was closed, and the source of leakage was a minute stitch opening, due to the injured tissue through which the suture passed. This case is, to some extent, analogous to Case v. The severe injury to the base of the bladder was, in each instance, repaired satisfactorily, excepting for a small postoperative fistula. In Case v the fistula occurred on the line of union because of the presence of an exposed and corroded needle. In Case vi it occurred between the line of union and the pubic arch as the result of repeated passing of the needle at this point, where the tissue was thin and weak. The repair of the small opening in Case v was done without difficulty, and in Case vi, should the closure of the minute opening be deemed desirable, it can be done with the same certainty of success.

The closure of the urethral fistula was not attempted in Case vi, as its direction was at a right angle to that of the vesical fistula, and to repair it would have added an unnecessary complication to the operation.

It is surprising that a surgical feat which held the attention of a large part of the surgical world for many years, and which brought to its author many national and international honors, should be today almost forgotten. The writings both of European and American surgeons of the present era are scant in their recognition of Sims and his work.

It is interesting to review Jellett's estimate of the techniques that have been used in the treatment of vesicovaginal fistula since the day of Sims. They are applied according to the character of the fistula. He states that "in cases of very small fistulae the best operation is that described by Mayo, in which the fistulous tract is dissected out and inverted into the bladder, the resulting flap being closed by sutures." The techniques of Sangar, Dudley and Mackinrod are suggested for special conditions; the latter is considered of particular value when the anterior vaginal wall is badly scarred.

Eden and Lockyer, after discussing the varied techniques which, in their opinion, might be used successfully in closing vesicovaginal fistulae, conclude with the following statement: "In the presence of urinary infection, success is very difficult to achieve." This statement is entirely in accord with the scientific teachings of today, yet, when we consider the facts, that the infected bladder was commonly associated with the vesico-vaginal fistula in the day of Sims, that Sims' technique, in his and Emmet's hands, gave results which, if ever equalled, have not been surpassed, and that these results were attained in a day of preaseptic surgery, it is indeed surprising that this technique is not given more consideration. These authors classify vesicovaginal fistulae according to their location; first, those located high in the vaginal vault; second, those located in the middle or lower third of the vagina. The first class, they think, "can best be reached by an intraperitoneal suprapubic operation," but they admit that such a procedure "is formidable owing to the difficulty in obtaining access to the parts." This comment is rational, whether the uterus has previously been removed or not. During my many years of practice I have frequently encountered vesicovaginal fis-

* "My dear Dr. Bissell:

You will be interested to know that your vesicovaginal fistula case, Mrs. W, continues to do well—the condition having changed none in the last six months. There is an invisible hole which leaks urine very slowly. She voids in large amounts and is able to hold her urine all night without wetting the bed. There is only a very moderate amount of moisture at the vulva and there is no excoriation. It does not bother her enough to think of any further operative work. She is most grateful for all you did for her, as am I.

Very sincerely yours,
James R. Miller.

October 5, 1928.

tulae at the vault of the vagina, but have never found it necessary to resort to so radical a method. Three of the fistulae included in this article (Cases I, II, and IV) were located at the vault of the vagina. Cases I and II might have been approached per abdomen; Case IV could not have been so approached without first removing the entire uterus, and, as the cervix was in the bladder and occupied the region of the trigone, an operation to remove it per abdomen would truly have been most formidable. I am unable to conceive of a vesicovaginal fistula so situated as to make the abdominal route preferable to the vaginal. Such cases may exist, but my experience would, I think, direct me first to a trial of Sims' technique before adopting a far more complicated and dangerous one; and may I here again remind you that fistulae, located in the vaginal vault with the cervix in the bladder, were met with in the days of Sims and Emmet, and were treated successfully by this technique.

With regard to the second class of fistulae, or those located in the middle or lower third of the vagina, Eden and Lockyer consider two methods applicable; first, "the edges of the fistula are simply rawed and then stitched together; second, a flap-splitting technique, where the bladder and the vaginal walls are first widely detached from one another, and then separately united by individual sets of sutures." The first method of procedure simulates that of Sims, but as, in the opinion of the author, it is not applicable to large fistulae, and Sims' technique is applicable to both large and small, it would seem that in this first method there is wanting some essential element, which I judge to be the silver wire suture. The second, or flap-splitting method is considered applicable to large fistulae located in the middle or lower third of the vagina. It is presumed that fistulae at the neck of the bladder are here included. The flap-splitting method is applicable to a large majority of fistulae located at the base of the bladder, and should always be chosen by those not familiar with the Sims technique. However, when a vesicovaginalfistula is so extensive as to permit of the cervix entering the bladder and there becoming fixed, thus forming part of the vesicovaginal septum (as in Case IV), we have, it would seem, a condition not suitable for the flap-splitting method. Again, when destruction of tissue is encountered at the neck of the bladder to the extent met with in Cases V and VI, the flap-splitting method is not applicable, for the dense scar tissue at the base of the urethra presents an insurmountable difficulty. In Case VI there existed, in addition to the scar tissue at the base of the urethra, an urethrovaginal fistula 1 cm. in length, and, as the preservation of the bridge of tissue between the vesicovaginal fistula and the urethrovaginal fistula was essential to success in the repair of the vesicovaginal fistula, any operation which destroyed its continuity would inevitably have met with failure.

If my opinion were to be solicited as to the greatest living American authority on gynecology, I would unhesitatingly say Howard Kelly, for in him there is consummated a knowledge, both theoretical and practical, of all the divisions of the art and science of medicine which, in a broad sense, constitute gynecology, i.e., obstetrics, urology and the study of diseases peculiar to women. In a recent issue of his "Surgical Gynecology" he devotes considerable attention to the subject of vesicovaginal fistula, and lays down certain fundamental principles in the midst of which he interjects a comment in which he states that Sims' technique for the cure of vesicovaginal fistula was applied by Sims and his early followers under circumstances most disadvantageous, yet with almost uniform success. In so doing, Kelly admits that the technique is not only sound in principle but universal in application. He concludes, however, by saying that a knowledge of its use has virtually passed away.*

* Kelly's comment on Sims' technique is interesting: "Our forefathers, especially Sims and Emmet, succeeded under conditions of extreme awkwardness, where we today, with less of their special skill wrought out of an abundant experience, would fail lamentably.

Half a century ago the name of Marion Sims stood foremost among American surgeons. His clinical work was known and appreciated, not only by his Countrymen but also by his fellows of Europe. His book, "Uterine Surgery," was the first publication on this subject by an American, and created a great interest in the specialty throughout the medical world. Yet, within a quarter of a century after his death, his outstanding surgical feat was overshadowed by discoveries and achievements in other departments of the field of medicine which redirected the course of surgery.

During the era in which Sims lived, surgical knowledge was limited to mechanics and individual dexterity, and had not medical knowledge advanced in the direction of pathology and bacteriology, morbidity and mortality would have continued to be what they were in the days before Lister. Sims, however, in spite of the lack of the knowledge of asepsis or antisepsis, succeeded in combating conditions where others failed. The methods (other than that of Sims) employed today in curing vesicovaginal fistula, when successful are so, not because of their superior mechanics but, because of a knowledge of sterilization, as applied to material and the operative field; and had not Lister, or some other equally great benefactor, shown the way to the successful combating of the causes of infection, the techniques which utilize buried sutures would not be given consideration.

Sims' great achievement was not that which is so commonly but erroneously attributed to him, namely, priority in the cure of vesicovaginal fistula, but it was that of perfecting and popularizing a technique which was simple in principle and more nearly universally applicable than any technique devised previous to or since his time. The use of the silver wire suture was the chief feature of this technique, and the almost uniform success attained by Sims and Emmet demonstrated that when it was correctly applied primary union became the rule and not the exception. It is of interest to observe, further, that this fact was of greater import than at first appeared, for, when the silver wire suture technique was applied to other birth-canal injuries, the results were incomparably better than those which had previously been obtained.

Although Sims did not discover nor popularize a single principle which changed the course of surgery, yet his name must always be associated with the advancement of the art and science of medicine, for he raised the operative standard to a higher plane than that on which he found it.

My hope is to awaken interest in a subject which has, seemingly, passed into history as only a stepping-stone in the progress of surgery. Sims' achievement was more than a stepping-stone; and my belief is that while other techniques can be applied under special conditions, Sims' is universally applicable, and he who has it at his command is thereby enriched. It is too valuable to be discarded, and my effort is not only to arouse interest in it, but to reestablish it in the armamentarium of the gynecologist.

Like the bow of Ulysses, there is scarcely one today who can handle these tools or use their legerdemain in this field. However, we can congratulate ourselves in the possession of methods and devices not available in their day; short-cuts and by-paths over the rough roads to success."

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END RESULTS OF EXOPHTHALMIC GOITER*

ROBERT C. AUSTIN, M.D., F.A.C.S. AND H. H. WAGNER, M.D.

DAYTON, OHIO

THIS presentation is based upon a clinical and histological study of 192 cases of exophthalmic goiter that we have operated upon and followed by clinical and metabolic examinations. For this study the great majority have been checked clinically and in addition have answered form letters. This investigation was to learn (1) the relation between the degree of hyperthyroidism and clinical result; (2) the relation between the duration of the disease and clinical result; (3) the relation between the degree of involution following iodine medication and end result; (4) the relation between iodine therapy preoperatively and postoperatively to postoperative basal metabolism readings and (5) finally the end results in terms of rehabilitation of the patients.

One may say with emphasis that the basis of sound treatment of hyperthyroidism is an accurate diagnosis. While it may be easily determined there is no clinical situation in which one may have greater difficulty in differential diagnosis as in thyroid states. The borderline hyperthyroidism, the low grade pulmonary infection and the neuroses tax the clinical resources of the most experienced observers.

Several factors have contributed to the very low operative mortality which but a few years ago was formidable: (1) meticulously made diagnosis, (2) careful preparation in which Lugol's solution is the most important adjunct, (3) good surgical judgment as to the ability of the patient to withstand surgical stress and the adaptation of the proper surgical procedure to his needs, (4) the displacement of ether by local anesthesia or preferably the combined local and gas anesthesia, (5) good surgical technique and, not the least, an alert postoperative supervision that can anticipate a crisis and prevent it.

The hyperthyroidism cases in this group were graded on a scale of 1 to 4 and varied in terms of basal metabolism readings from slightly above normal to +108. It was a reasonable supposition that the severe cases of hyperthyroidism would be attended with more sequela of injury to the heart, kidneys, blood vessels and nervous system. Our study in the end results in this group showed, surprisingly, as high a percentage of cures and satisfactory results as did those of a lesser degree of hyperthyroidism. They required a longer convalescence varying often from six months to a year. A group of 6 of the severest hyperthyroidism cases with metabolisms varying from +70 to +108, whose operations were attended with the severest reactions, but whose histories showed less than six months' duration, reported that they were well after an interval of a year. Another group of a lesser degree of hyperthyroidism, but of a longer duration (one year or more) presented more residual symptoms of nervousness, some fatigability, dyspnea and palpitation upon exertion. Our conclusions confirm those of other writers that patients who are cured of their hyperthyroidism early in the disease, despite its severity, have a high percentage of good end results.

The relation between the degree of involution and end results was in conformity with the report of Drs. Simpson and Arn. We reviewed the cases in which the pathological report stated that there had been a lesser degree of involution than usual or a lesser response to iodine. Four of 6 recurrences in this group of 192 cases showed a poor response to iodine. In 3 of the 4 recurrences there was, according

* Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929.

to our operative records, a larger amount than usual of thyroid tissue left during resection. A patient who has had a lesser clinical response to iodine which is parallel to the involutionary changes demands apparently a removal of a greater amount of thyroid tissue. The study of this group of cases has not given me any reason to alter my opinion that a sufficient removal of thyroid tissue will cure Graves' disease.

We have believed from clinical observation that iodine preoperatively and continued postoperatively had an influence towards a lower postoperative basal metabolic rate. Our study revealed that it was the usual occurrence for a patient of this group to have, three months after operation, a basal metabolism reading below normal, varying from 0 to −6, −8, −10, and as low in a few cases as −16 and −20. In contrast the earlier cases, before the advent of Lugol's solution, rarely had a basal metabolism reading below normal postoperatively and averaged 10 points higher than the group in which Lugol's solution was used.

Since Marine gave us convincing evidence that iodine tended to control hypertrophy and hyperplasia we have used it routinely in the postoperative program. We have in the period of preparation administered 30 to 60 drops per day (average twelve days); in the first six weeks of the postoperative period 10 drops per day and in the subsequent six weeks, 5 drops per day; thereafter 15 drops per week or its equivalent, 1 tablet of iodostarine containing 10 mgs. of iodine every other day.

We have too, applied the program of maintaining the proper postoperative balance to the colloid adenomatous group. I have not seen a single patient of either group who has been harmed by it and I believe that it tends to keep the thyroid normal and to prevent recurrences.

This opinion is confirmed by Marine and Else. Marine early in his investigations stated that iodine tended to control hypertrophy and hyperplasia and he later confirmed it by animal experimentation. Else, in an early report two years ago and in a later one last year showed that if a maximal or reasonable amount of thyroid is left, no hypertrophy or hyperplasia takes place. If a little more is removed, hyperplasia and hypertrophy take place and is not influenced by iodine, and often as a result of the stimulation to the small remaining area of thyroid tissue regeneration followed. A case of recurrence: S was operated upon six years ago, a bilateral hemithyroidectomy being done following ligations, and according to his record a very small amount of thyroid tissue was left on either side. He was a hard physical worker in the American Rolling Mills at Middletown, working under great stress. He returned with a moderate hyperthyroidism and a right lobe of size 2 plus. He had had a regeneration. While Marine and Else have shown us that iodine is important in maintaining normalcy in the thyroid gland preoperatively and postoperatively, iodine administration will not prevent a recurrence if an insufficient amount of thyroid has been removed. Three of 6 recurrences in this group had taken iodine postoperatively.

A fact that must be emphasized is that iodine is not a cure for exophthalmic goiter. Its administration does result in an involution of the gland. We mean by involution a decrease in vascularity, a decrease in the height of the columnar epithelium, an increase in the colloid, an increase in the size of the acini with a more regular contour of the border, an increase in the connective tissue and a decrease in the lymphoid hyperplasia. This involution is marked in 90 to 95 per cent of cases and the basal metabolism reading is relatively improved. The height of maximum clinical improvement is reached in about ten to twelve days with the administration of 30 to 45 drops of Lugol's solution daily. An important clinical fact that deserves to be emphasized is that if iodine is continued the patient may have a remission and that the opportunity to

operate on the patient at the moment of maximum improvement is lost.

While I do not intend to discuss adenomatous goiter it is apropos to state that we have found the results of iodine beneficial as a preoperative measure in this type of goiter, though not as spectacular as in the Graves' disease. I have not seen a patient of the toxic adenomatous group with a moderate or severe hyperthyroidism whose symptoms have been aggravated and in the majority of cases the benefit is definite.

Hyperthyroidism is inseparably associated with hyperplasia and hypertrophy, be it in the Graves' or adenomatous type and it is a logical as well as a practical conclusion that iodine is beneficial to each.

Ninety-four per cent of this group have had satisfactory results in terms of rehabilitation without a mortality. While this study reveals some imperfections in the surgical treatment of goiter, the conclusion is evident that operative results as compared with other programs of treatment are highly satisfactory.

CONCLUSIONS

1. Exophthalmic goiter patients who are cured early of hyperthyroidism, despite its severity, have a high precentage of good end results.

2. Patients who have had a poor response to iodine as expressed by a lesser degree of involution and a lesser clinical improvement are more prone to have residual symptoms or to have recurrences.

3. Patients given iodine postoperatively maintain a lower basal metabolic rate.

4. Surgical end results are in a high percentage satisfactory.

THE INDIVIDUALIZATION OF GOITER PATIENTS*

WILLARD BARTLETT, M.D., F.A.C.S., AND WILLARD BARTLETT, JR., M.D.

ST. LOUIS

THE extent to which it had become necessary to individualize in the care of goiter patients in our clinic was first called to our attention in surveying the following list of cases presented in May, 1928, for the Southern Society of Clinical Surgery:

1. Psychosis in toxic adenoma.
2. Laryngeal complication after operation.
3. Organic heart lesion with exophthalmic goiter.
4. Bronchiectasis with toxic adenoma.
5. Diabetes with toxic adenoma.
6. Acute thyroiditis in parenchymatous goiter.
7. Low basal rate with highly toxic mixed type goiter.
8. Recurrence of exophthalmic goiter.

The wide variation in the methods of preparation and in the types of operation best suited to each patient called to our attention the inadequacy of a routine in dealing with cases whose individual needs were so different. It is true, of course, that such a list does not represent the proportions in which such cases occur in a large series; however, they are representative of the many in the hospital at that time. It is now our conscious effort to draw on as wide a range of operative procedures as may be necessary, each of which takes into account special features of the physical and psychic problem presented.

The non-toxic patient is ordinarily dealt with in one of two ways: the first of these is bilateral resection according to the method, with slight individual variations, in general use, with complete closure of the incision. This we regard as being the "ideal operation." The second method is designed to meet unusual mechanical problems and its essential difference from the ideal operation is that the retraction of all tissues is in a longitudinal direction rather than lateral from the midline. The usual collar incision is made through skin and subcutaneous fat, and upper flap retracted; 3 cm. above the skin incision and parallel to it all the remaining tissues of the neck are divided transversely including the anterior edges of the sternomastoids. Retraction, then, of upper and lower flaps gives one exposure of a field particularly adapted to (a) the removal of a very large goiter, (b) an intrathoracic goiters, since mobilization of their upper poles allows them to be "skidded up" along the tissue planes, (c) short necks in whom the transverse plane is greater than the longitudinal one.

Of the three operative procedures for toxic patients the first to be described is the one most frequently used. Its various steps follow those of the bilateral resection on non-toxic cases up to the beginning of closure. A voluminous soft rubber pack is inserted on each side, the cervical fascia pulled together over the trachea with one suture, the subcutaneous fat approximated in the midline with one or two sutures, and the skin edges approximated in the midline with one or two mattress sutures allowing the rubber drains to protrude from each side of the incision, giving these cases the primary requisite, drainage, as first recognized by Dr. Crile. These wounds do not require secondary closure, and on seeing the patients months later it is frequently necessary to consult their records to find out whether or not they were drained at operation.

The second operation for toxic cases is a bilateral resection in two stages and is designed to deal with the not inconsider-

*Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929.

able number of patients whose ability to go through a complete operation cannot be predicted until they are on the operating table, and in some cases until the operation actually begins. By the method to be described we are able to interrupt the operation should pulse, blood pressure, or other vasomotor symptoms be suddenly increased. The usual collar incision and midribbon muscle split are made; the cervical fascia nicked high on each side; all bleeding points are then carefully ligated; the four points formed in the cross-divided cervical fascia are sutured with one stitch; the superficial fat pad approximated, and the skin completely closed without drainage to seal the wound against infection. Secondary operation can then be performed from three to ten days later although the ideal time is at about six days. One then goes immediately through a bloodless field onto the gland. This is above all an operation of expediency for unpredictable cases.

The third operation for the toxic patient is a predetermined unilateral resection with which we have been able to extend the limits of operability to include many cases in whom we should have otherwise had to choose between turning them away or risking their lives. It is for the frequent desperate case whose margin of safety is very slim. As done in the male subject, the skin incision is made over and parallel to the sternomastoid and this incision continued down through all the layers, bringing one directly onto the upper pole; the exposed lobe and sometimes the isthmus are resected; a voluminous soft rubber pack placed in the defect, and the skin caught at the middle of the incision with one mattress suture, allowing the drain to protrude on either side of it. Since such a scar would be quite disfiguring to a woman, particularly a young one, for them half a collar incision is made through the skin, and retraction on the upper and lower flaps exposes the sternomastoid muscle through which exposure of the gland is carried out as before.

The following outlines of three patients dealt with by the method last described will give some idea of how desperately sick these individuals were and of what sort of course can be expected of them.

Case I. Mrs. O. K., aged forty-nine.
Diagnosis: Mixed toxic goiter.
Type: Gastroenteric and nutritional predominating.
Admitted: April 22, 1928.
May 22, 1928: Symmetrical exposure.
June 2, 1928: To operating room; unfit for operation.
June 11, 1928: Roentgen-ray treatment.
June 12, 1928: Roentgen-ray treatment.
Discharged: June 16, 1928.
Readmitted: September 13, 1928.
October 6, 1928: Primary lobectomy (rt).
October 15, 1928: Complete paralysis right vocal cord.
Discharged: October 27, 1928.
Readmitted: April 3, 1929
April 10, 1929: Secondary lobectomy.

A year elapsed between this woman's first admission to the hospital and the completion of her operation. It will be noted that on May 22, 1928 a bilateral resection was tentatively scheduled but she reacted so badly on the table that the operation was divided and only the exposure of the gland, as described, was carried out. Eleven days later an attempt was made to finish the operation, but again it became clear that she would not stand it, and she was returned to her bed. After three months at home she reentered, having gained 15 pounds, and primary lobectomy was carried out six months after she was first seen. Following this she improved so much in every way, in spite of the paralysis of the right vocal cord, that secondary lobectomy was carried out six months following the primary lobectomy, and at the time of this writing the patient is one week postoperative and doing well.

Case II. Mrs. G. C., aged fifty-four.
Diagnosis: Toxic adenoma thyroid.
Type: Nutritional, *later* cardiac.
Admitted: June 7, 1928.
July 6, 1928: Symmetrical exposure.
Discharged: July 18, 1928.
Readmitted: November 23, 1928.
December 2, 1928: Influenza.
Jan. 10, 1929: Diphtheria; isolation hospital.

January 23, 1929: Returned to ward.
February 16, 1929: Primary lobectomy (rt).
Discharged: March 9, 1929.

It is worthy of note that nearly nine months elapsed here between first admission to the hospital and primary lobectomy. She is now at home on a strict regime and we are awaiting the coming of warm weather to have her return for secondary lobectomy, if such be possible.

Case III. Mrs. M. T., aged fifty-four.
Diagnosis: Mixed toxic goiter.
Type: Cardiac decompensation predominating and nutritional.
Admitted: June 28, 1928.
August 4, 1928: Primary lobectomy (rt).
Discharged: August 16, 1928.
Readmitted: October 8, 1928.
October 13, 1928: Secondary lobectomy.
October 14, 1928: Tracheotomy (complete bilateral paralysis of cords).
Discharged: October 30, 1928.
Office: March 18, 1929. Had gained 45 lbs.

At our primary lobectomy here we evidently got a unilateral paralysis which was not detected until immediately after the secondary lobectomy two months later. The damage done on the left, the second side, was only temporary, happily, and when reexamined five months after her last operation she had a good voice but wheezed a little after exertion.

It will be deducted from the foregoing that general rules to fit all cases can scarcely be formulated for goiter patients; on the other hand, we feel that our experience has led us to evolve six methods of procedure when confronted by a goiter patient who is also in need of a second surgical operation as well as a thyroidectomy. We are inclined, in most instances, to perform the thyroidectomy first (1) if inhalation anesthesia is required for other operation; (2) if patient is highly toxic; or (3) if goiter symptoms seem the more important.

Without wishing to belittle the need or importance of a thyroidectomy in another group of patients, we perform, or at least advise the *other* operation first (4) if for malignant lesion; (5) if to eradicate a source of infection; or (6) if it entails the longer hospital stay.

These rules are, of course, not universally applicable although they will be found workable in the large majority of patients. It may be stated that there is an exception to number (5) so far as the tonsils are concerned. We have always regretted having a tonsillectomy precede the thyroidectomy.

NODULAR GOITERS: THEIR RELATION TO NEOPLASIA*

ALLEN GRAHAM, M.D., F.A.C.S.

CLEVELAND

ENLARGEMENT of the thyroid gland tends to develop in individuals living in localities where endemic goiter abounds. The incidence of persons thus affected varies with the factors which may be regarded as determining the intensity of the endemic influence. Among the factors generally considered as having an important causal relationship, the following may be mentioned: heredity, age, sex, social status, economic conditions, hygienic and dietary insufficiencies, and finally, but probably not the least important, an inadequate amount of iodine available in the air, water or food, or an inability to utilize iodine when it is present. The resulting enlargement of the thyroid, in the early years of life, is usually diffuse and uniform, without nodules or neoplasms. With advancing age and in direct relation to the intensity of the endemic influences, an increasing percentage of the thyroid glands which in early life were diffusely and uniformly enlarged become irregular, lumpy, nodular, or adenomatous (neoplastic). (Fig. 1.)

These are well-established facts that have been attested by practically all authorities who have concerned themselves with the subject of goiter. They will serve very well as a starting-point for a discussion of (1) the process by which the presumably normal or at least non-nodular thyroid becomes transformed wholly or in part into a structure that is nodular; and (2) whether the resulting nodules are neoplastic or non-neoplastic. Inflammatory nodules and malignant neoplasms are excluded from this discussion.

I. THE ORIGIN OF NODULAR GOITER

A. *The Embryonal Rest Theory.* According to Wölfler's[2] view, which met with rather general acceptance for many years, the nodular goiters, or as he considered them, the adenomata of the thyroid, developed from embryonal rests persisting from the fetal period of life. The implication was that portions of the original anlage of the thyroid, which under normal circumstances should undergo a physiological involution, atrophy or resorption, failed to disappear and remained as islands of embryonal tissue. These embryological remnants might remain dormant or, for some unknown reason, begin to grow at any subsequent period of life. This was considered to be the origin of these encapsulated nodules which were designated as "fetal adenomata."

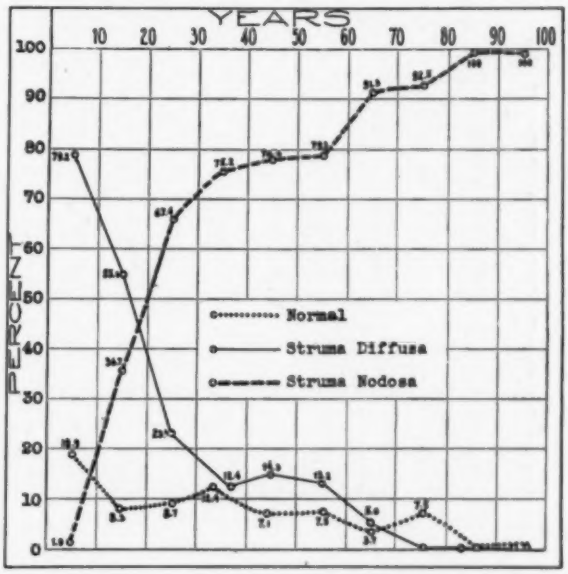

FIG. 1. Chart showing percentage of normal thyroids, diffuse goiters, and nodular goiters in different age-decades, as calculated from findings in 696 consecutive necropsies. Adapted from C. Wegelin.[1]

Irrespective of the correctness of Wölfler's view as to its origin (an alternative conception will be suggested later),

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the lesion described by him as fetal adenoma has been recognized ever since. In its purest form it consists of a circumscribed or encapsulated mass (Fig. 2) of immature or relatively undifferentiated, non-lobulated thyroid tissue, having a histological appearance which is exactly similar to the thyroid of a fetus of a certain age, except for absence of lobulation. As long as this lesion conforms to the foregoing specifications there will probably be little difficulty as to its recognition.

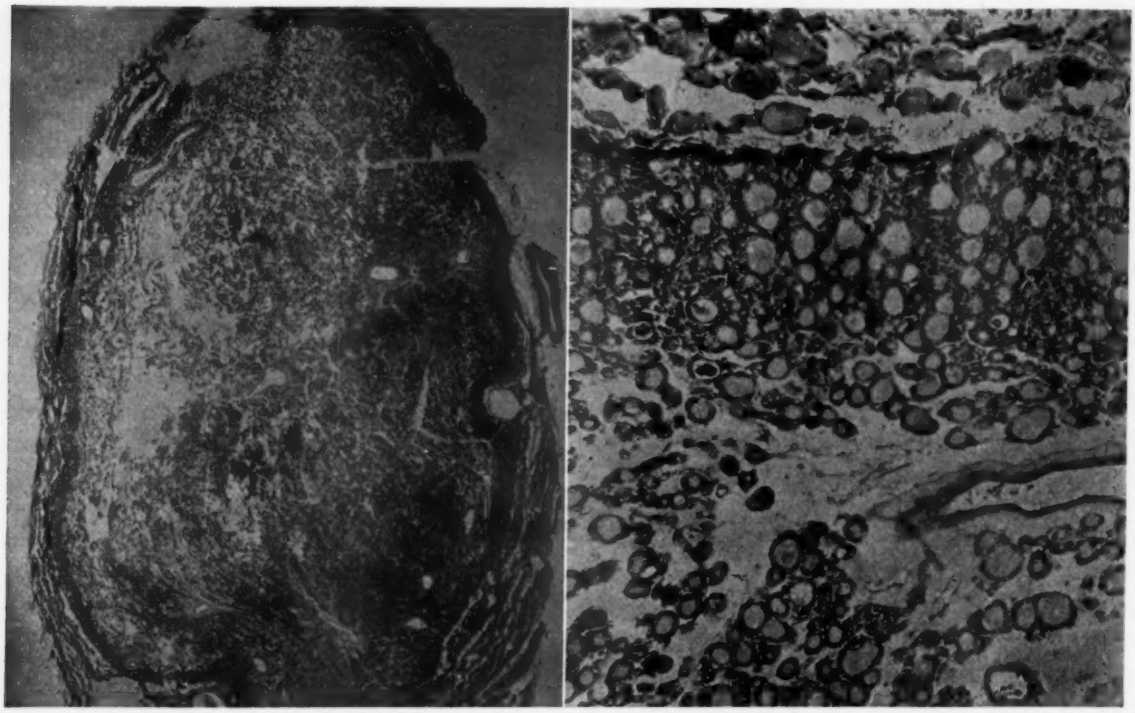

Fig. 2. Encapsulated nodule in colloid goiter, showing non-lobulated "fetal" structure (so-called fetal adenoma).

Experience has demonstrated beyond question, however, that this lesion does not necessarily remain in its original state of development. It has not only an obvious capacity for growth, but an equally obvious capacity for differentiation. By this I mean that the fetal adenoma, which at first has the morphological characteristics of the thyroid of a fetus, in the natural course of events tends to have the morphological characteristics, except lobulations, of the normal thyroid of an adult. (Degenerative changes are secondary and will not be considered here.) All the stages in the process of differentiation may be encountered in a series of thyroids, or even in a single gland. Moreover, all the stages in the transition from adenomatous tissue of "fetal" type to adenomatous tissue of adult type may be encountered in a single encapsulated nodule. (Fig. 3.)

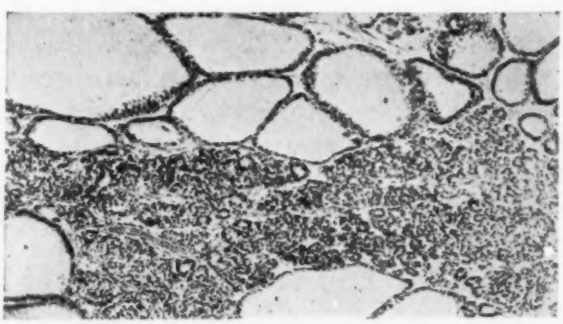

Fig. 3. Section showing intimate admixture of fetal (relatively undifferentiated) and adult (fully differentiated glandular tissue in same encapsulated nodule.

Along with the process of morphological differentiation there is the acquisition of qualities of a chemical, pharmacological, physiological, and biological nature exactly

comparable to similar qualities pertaining to fully differentiated adult non-tumorous thyroid tissue. Among these may be mentioned the accumulation of colloid in the acini; the fixation, conversion and storage of iodine; the elaboration of the active principle or hormone of the thyroid; the capacity for hypertrophy, hyperplasia and involution of the acinal epithelium; the capacity of the desiccated adenomatous tissue to induce premature metamorphosis of tadpoles, a capacity which in a general way is directly proportional to the iodine content of the adenomatous tissue.

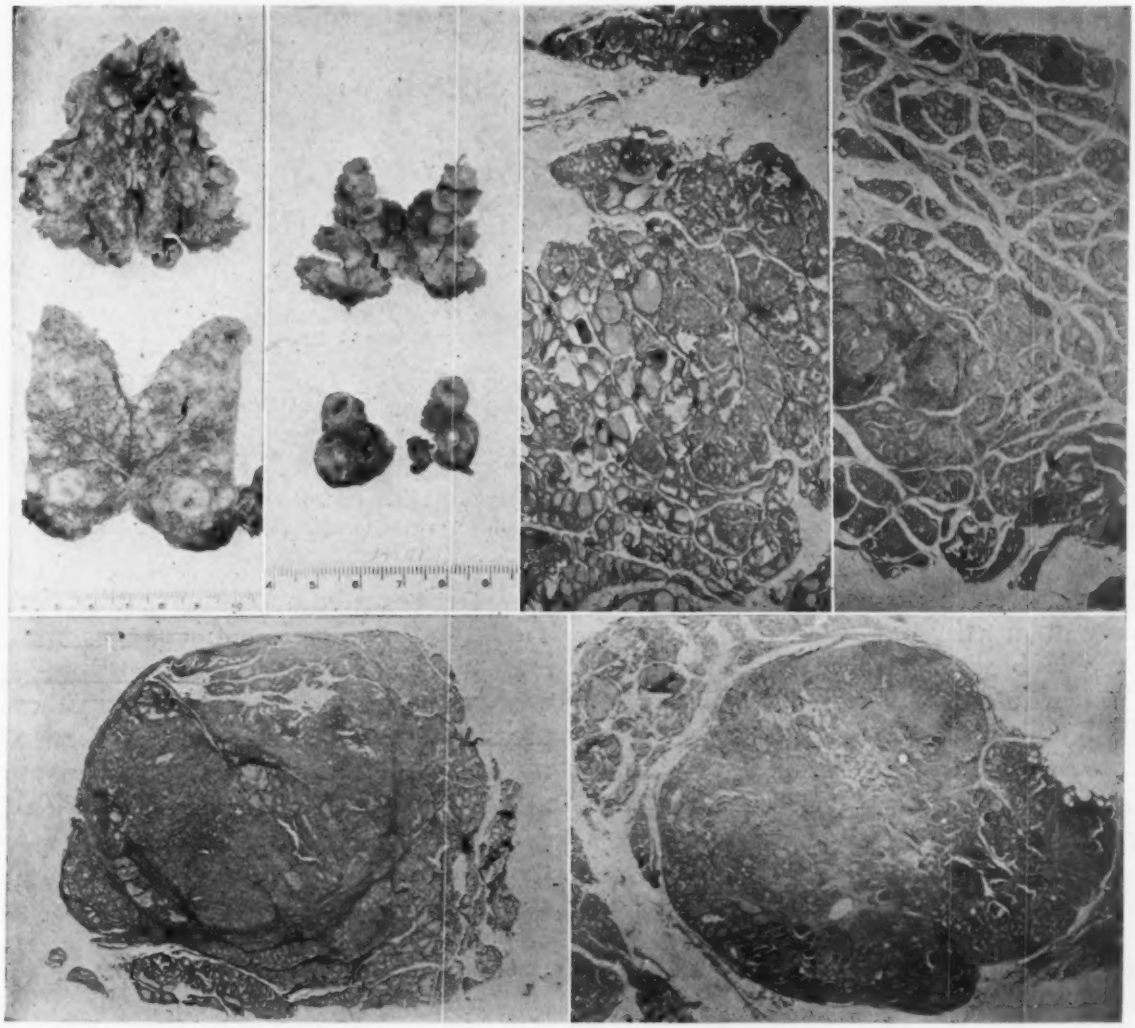

Fig. 4. Hyperplastic thyroid tissue from case of exophthalmic goiter, showing various stages in process of nodulation: nodular hyperplasia to encapsulated adenomata.

B. *The Theory of Irregular Hyperplasia and Involution.* In contrast to Wölfler's theory is the one which ascribes the development of nodular goiters to a process of irregular hyperplasia and involution, irregular isolation, circumscription and final encapsulation occurring in persons whose thyroids for various reasons have undergone spontaneous enlargement and have remained enlarged for long periods of time.

That nodular goiters may develop in accordance with the process or mechanism implied in this theory is borne out by considerable direct objective evidence, and many investigators have supported this view. It is not difficult to obtain visual indications that such a process takes place in

the thyroid; hence this theory is further removed from the realm of pure speculation than is the theory of embryonal rests.

follows: The localized area increases in size by further proliferation of tissue. With increasing growth more and more

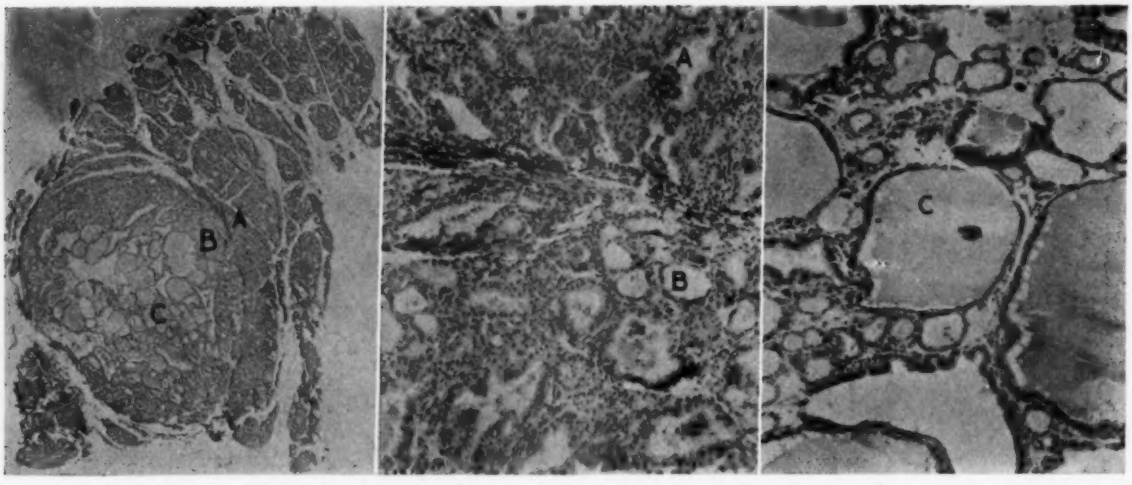

Fig. 5. A. Hyperplastic non-nodular thyroid tissue. B. Hyperplastic peripheral zone of encapsulated nodule, histologically indistinguishable from A. C. Central zone of same nodule showing numerous large colloid-filled vesicles.

The process of transition from normal, non-nodular thyroid tissue to nodular goiter is best exemplified in the glands of individuals who are approaching or who have attained adult life, or at least are well beyond the period of puberty. The end results of the process are best exemplified in later life. Both the process and the end result obtain their most complete anatomical expression in regions in which goiter is endemic. The process is well known in man and has been observed in some of the lower animals.

In the earliest stages nodulation of the thyroid begins with a localized area of hyperplasia, with the formation of new glandular structures, with increasing lack of orderly arrangement, with increasing demarcation (Fig. 4) between the localized area and the surrounding tissue, with failure of development of the stroma and lobulation that characterizes normal thyroid tissue. The parenchyma of the localized area may be indistinguishable (Fig. 5, a and b) from the surrounding lobulated non-nodular thyroid, or it may differ (Fig. 5, c) markedly from the latter.

The subsequent course of events is usually considered to be somewhat as pressure is exerted upon surrounding tissue. This results in atrophic changes in the immediate vicinity, replacement fibrosis of the portions undergoing atrophy, compression and consolidation of the zone of replacement fibrosis, and the final development of what must be considered as a capsule of a mass of non-lobulated thyroid tissue. Between these encapsulated masses and the earliest changes noted in the non-nodular thyroid there is nothing left to the imagination in the way of transitional stages.

c. *The Relative Merits of the Embryonal Rest and the Hyperplastic-Involutional Theories.* We are confronted with the necessity of choosing between the following propositions: (1) All nodular goiters develop from embryonal rests. (2) All nodular goiters develop by a process of irregular hyperplasia and involution. If either one of these two propositions can be established, it will not be necessary to consider the third theoretical possibility, namely: (3) Some nodular goiters develop from embryonal rests, while others result from irregular hyperplasia and involution.

The proposition that all nodular goiters develop from embryonal rests is untenable

for the reason that numerous investigators have been able to demonstrate a direct transformation of thyroidal epithelium into

it could not be considered as proved that the islands were remnants of the original anlage or duct system of the thyroid.

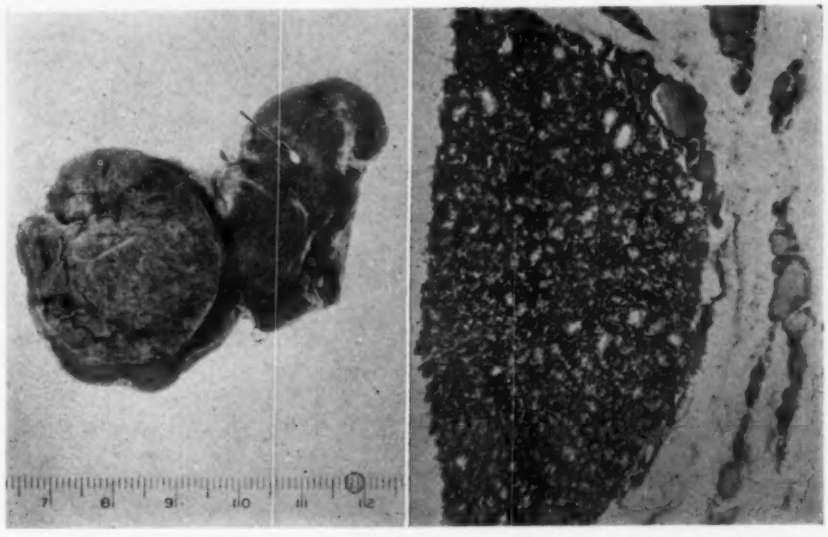

Fig. 6. Left: Large colloid adenoma in isthmus; small white nodule (1 mm. diameter) in lateral lobe of colloid goiter. Right: Photomicrograph (× 125) of white nodule. Note scarcely detectable capsule, "fetal" appearance of tissue histologically, and absence of degeneration.

encapsulated masses, with which observation my own experience is in accord. This, however, does not entirely eliminate embryonal rests as a possible source for certain nodular goiters or for certain types of nodules. The lesion *par excellence* which seems in accord with Wölfler's theory is the nodule known as fetal adenoma.

The term "fetal adenoma," however, carries with it an implication as to origin which may not be entirely justified. There are important considerations which are difficult to reconcile with Wölfler's theory.

Subsequent investigators, even in the most intensely goitrous districts, have had great difficulty in recognizing embryonal rests in the thyroids of embryos, infants, or children in the first few years of life. Certainly the difficulty of detection of embryological remnants is out of harmony with the incidence of "fetal adenomata" in adolescence and adult life.

Even if it were possible to demonstrate that all fetal adenomata developing at the age of puberty or thereafter represent further growth of islands of tissue that were present in the thyroid of the fetus, *It would still be not inconceivable that the islands of tissue in the fetal thyroid might be the result of the same mechanism as that which is responsible for the development of localized areas of hyperplasia (nodules) in the adult thyroid.*

This brings us to a consideration of the important question upon which the tenability of Wölfler's theory depends, namely, *can the fully differentiated adult thyroidal epithelium revert (de-differentiate) to such a degree that it resembles the thyroid of a fetus?* If so, the lesion known as fetal adenoma may be entitled to this designation only by reason of its morphological appearances, and may not necessarily be dependent upon an embryological defect for its origin.

In favor of such a probability is the occurrence in markedly hyperplastic thyroids of minute areas which are scarcely visible to the unaided eye and are morphologically indistinguishable from classical examples of so-called fetal adenomata. These small areas may not have the slightest indication of a true capsule and may not present notable degenerative

changes, two features that are the rule rather than the exception in the case of thyroid nodules that have been present since birth. Moreover, the small solid nests, cords, and "fetal-like" acini may be found scattered among the original thyroid gland structures in such a manner as to indicate strongly their origin from the latter. They give the distinct impression of neoformations originating *in situ* from the original thyroid tissue and may have none of the usual indications of longstanding lesions. In a single thyroid these localized areas may be seen in all stages of transition up to large encapsulated benign neoplasms. They are to be observed not only in hyperplastic goiters (Fig. 5) but also in partially and completely involuted glands (iodine medication). (Figs. 6, 7.)

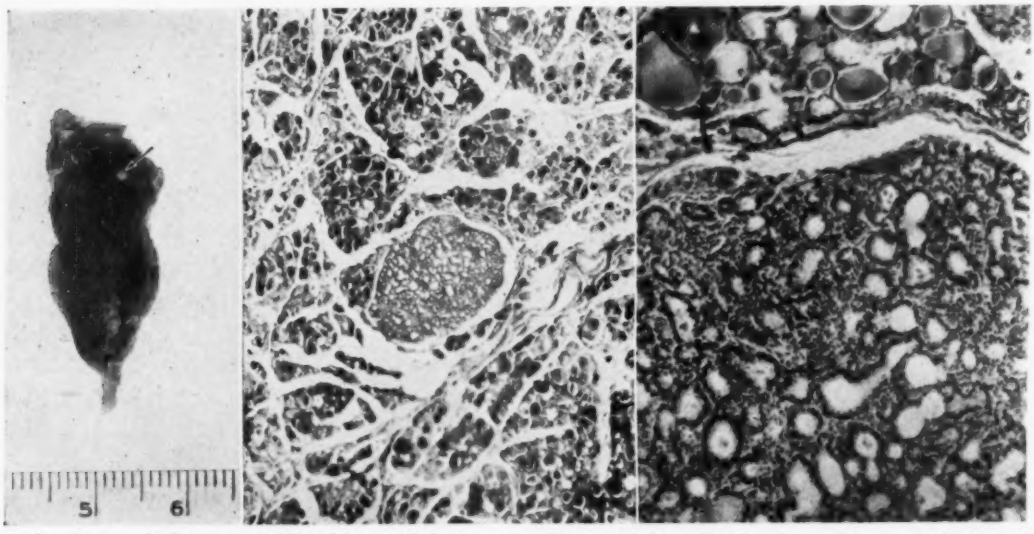

FIG. 7. Left: Arrow indicates small white nodule (1 mm. diameter) in colloid goiter. Center: Lobules of thyroid in relation to nodule. Right: Photomicrograph (× 125) showing fetal appearance of nodule.

Not all the nodules in a given thyroid are of the same age. Some are obviously of recent origin while others are obviously of longer duration. In this connection we can but speculate as to the relative importance in the development of nodular goiter of the intensity and duration of a single stimulus to thyroid overgrowth, and of repeated or recurring stimuli.

The foregoing considerations warrant the following inference: Since the development of benign nodular goiters of all types and descriptions, undifferentiated, partially differentiated, and fully differentiated, fetal and adult, is primarily dependent upon the development of endemic goiter, but is also known to be associated with such widely opposed states as hypothyroidism and hyperthyroidism, it is quite probable that the mechanism involved is intimately related to the one condition in the thyroid which is common to all three, namely, hyperplasia of the thyroidal epithelium. Involutional changes, whether spontaneous or induced, probably play little or no rôle in the initiation of the process but may modify the morphological aspects of the end result. The theory of irregular hyperplasia and involution offers an acceptable explanation for all types of nodular goiters occurring at all ages; it is supported by direct objective evidence; and is more removed from the realm of pure speculation than is the theory of origin from embryonal rests. The nodule known as fetal adenoma, which has been the most important objective support for Wölfler's theory, is not more satisfactorily explained on the basis of an embryological defect than it is on the basis of reversion, growth and differentiation of normal thyroidal epithelium. The degree of reversion and what occurs thereafter are, in all

probability, the important elements in determining the end result as we see it clinically, at operation, or at necropsy.

It is to be emphasized that rejection of Wölfler's theory concerning the origin of nodular goiter has no bearing on the question of embryological defects in the thyroid similar to those occurring in the thymopharyngeal tract and branchial apparatus, namely, cysts, fistulae, persistence of ducts, misplacement of tissue (aberrant) and the neoplasms which develop with relative infrequency in such defects. It is theoretically possible that some thyroid nodules might originate in embryological defects, but it seems a legitimate conclusion that this mode of development is of very minor importance in the development of nodular goiter in the usual sense.

II. THE NEOPLASTIC NATURE OF NODULAR GOITERS

Assuming that the end result of the process of nodulation is expressed anatomically by the localized masses of thyroid tissue frequently referred to as lobular hyperplasia, nodular goiter, adenomatous goiter, adenomatosis, struma nodosa, etc., and assuming further that this nodulation has its inception in a thyroid that otherwise is in no sense neoplastic, the question with which we are confronted is whether or not the process or the end result is to be considered as in any way related to neoplasia.

There are three possible views with reference to these questions: (1) All of the nodules occurring in goitrous thyroids are neoplastic (adenomatous). (2) None of the nodules occurring in goitrous thyroids are neoplastic. (3) Some of the nodules are neoplastic and others are not, or there is a transition from one condition to the other.

I know of no one experienced in the pathology of the thyroid gland hardy enough to deny the occurrence of true benign neoplasms (adenomata) in goitrous glands. On the other hand, within the past few years there seems to be a growing tendency to exclude from the group formerly classified as adenomata an increasing number of nodular glands on the ground that they are not neoplastic. For the sake of convenience in the present discussion we may designate the type of gland which has been excluded as nodular hyperplasia in contradistinction to adenomata or true benign neoplasms.

We are as far from having an acceptable definition of the term adenoma as we are from having a universally acceptable definition of the term neoplasm. In the absence of a satisfactory definition we may possibly accept the following as a basis for discussion: An adenoma is a mass of glandular tissue composed of the elements (with the possible exception of nerve supply) of the parent tissue or organ in which it originates, but not having the orderly or systematic arrangement or architecture of the parent tissue. It is a new growth, of unknown etiology, approaching the parent tissue in the degree of its differentiation. It is circumscribed or encapsulated, does not invade, exhibits little or no tendency to dissemination, and usually has little or no deleterious effect upon the general health. Moreover, it is characterized by a degree of independence or lack of restraint in its growth. Finally, it serves no useful purpose and is devoid of normal physiological function.

If it be agreed at the outset that certain nodules occurring in the thyroid are adenomata, it becomes necessary to determine what type of nodule may be accepted as such and to compare this type with the various nodular goiters that are not considered to be adenomata.

The so-called fetal adenoma (Fig. 2), the characteristics of which have been described in the first part of the paper, has met with the fewest objections as an example of a benign neoplasm. If this type of nodule be not a neoplasm, we are confronted with the paradox that a lesion of the thyroid which squarely meets all the requirements of the definition of a benign glandular neoplasm in other organs,

is to be excluded from that category. By what subtlety are we justified in excluding fetal adenoma of the thyroid from the category of benign neoplasms when we continue complacently to speak of fibroadenoma and adenoma of the breast, adenoma of the pituitary gland, adenoma of the adrenals, liver, kidney, prostate, testicle, ovary, intestine, etc. as benign neoplasms? Many of the last-named lesions are far less perfect neoplasms than are fetal adenomata of the thyroid.

If the so-called fetal adenoma be a neoplasm, some of the more or less ancient dogmas concerning certain features of the neoplastic process need revision. For example, unlimited, independent or unrestrained growth becomes a matter of degree rather than a total incapacity to delimit itself. It is difficult to recall any neoplasm that is absolutely unlimited, absolutely independent, or absolutely unrestrained in its growth. So far as natural phenomena are concerned, it is reasonably certain that the normal tissues of man have survived the ravages of time longer than has any neoplastic tissue; and so far as experimental observations are concerned, it is equally certain that normal tissues have been cultivated in vitro as long as has neoplastic tissue. This in no way implies that there is no difference between normal and neoplastic tissue as regards control or lack of control of growth; it is merely suggested that there is a limit to neoplastic growth.

Accepting as our type of benign glandular neoplasm the nodule generally recognized as fetal adenoma, and keeping in mind the foregoing definition of adenoma and the limitations indicated above as to unrestrained growth, we may contrast our type of neoplasm with so-called nodular hyperplasia, under the following captions:

Origin. Whatever view may be taken as to the origin of fetal adenoma, whether from embryonal rests or by a process of reversion, irregular hyperplasia and involution, it is obvious that it develops in and from tissue that originally is not neoplastic. We cannot conceive of a neoplasm apart from the tissue in which it originates. Neoplasms as such are not transmitted from generation to generation. *Both fetal adenoma and nodular hyperplasia originate in non-neoplastic thyroid tissue and therefore in this respect there is no fundamental difference between them.*

Differentiation and Morphology: In the developmental stages fetal adenoma is *relatively* undifferentiated, if we take the normal thyroid of an adult as our measure of full or complete differentiation. It is, however, no more undifferentiated than is the thyroid of a fetus of an age comparable to the morphological age, so to speak, of the neoplasm. However relatively undifferentiated the lesion may be, it cannot be denied that its natural tendency, in due course of time, is toward a degree of differentiation approaching and in many instances attaining (Fig. 3) that of the normal adult thyroid as regards its essential unit, i.e. the vesicle with its epithelium, colloid, iodine, and active principle.

Either the fetal adenoma differentiates as stated, or colloid nodules which are not fetal in origin revert to such a degree that portions of the neoplasm or nodule are morphologically indistinguishable from the thyroid of a fetus. This assertion is based upon the fact that fetal vesicles and colloid vesicles are frequently intermingled in the same encapsulated nodule (Fig. 3), whether benign or malignant.

The so-called nodular hyperplasias (Fig. 4), it is generally considered, originate in differentiated tissue. It is certain that in the process of nodulation associated with thyroid overgrowth some degree of reversion occurs. How far the reversion may proceed is possibly a debatable question. Examination of a large number of goiters strongly suggests that it may be complete. If it be so, the resulting histological appearances would be indistinguishable from those of the fetal adenoma.

It seems quite clear that the degree of differentiation or de-differentiation is not

an acceptable basis for distinguishing between so-called fetal adenoma and so-called nodular hyperplasia.

Functional Capacity and Usefulness. Proof of functional capacity in neoplasms has been furnished for both adenoma (McClenahan and Norris[3]) and carcinoma (Wilder et al.[4]) of pancreatic islet tissue, since in each instance the neoplasm was accompanied by hypoglycemia. An adenoma of the parathyroid associated with hypercalcemia has been reported recently (Barr et al.[5]). Previously it had been shown that premature metamorphosis of tadpoles occurred in a similar manner, whether the feeding experiments were undertaken with adenomatous (Graham[6]) or non-adenomatous (Lenhart[7]) thyroid tissue.

That the functional activity of neoplastic tissue may serve a useful pur- is indicated by von Eiselsberg's[8] famous case. Following total thyroidectomy symptoms of myxedema appeared; with the development of a metastatic nodule in the sternum the symptoms of myxedema cleared up, but they returned promptly after excision of the nodule in the sternum.

It is not intended to imply that functional capacity in neoplastic tissue is confined within what may be termed physiological limits, nor that it is under physiological control, nor that it is quantitatively the same as in normal tissue. It is merely suggested that neoplastic tissue can no longer be considered as totally devoid of functional capacity.

So-called fetal adenoma and so-called nodular hyperplasia are possessed of functional capacity in varying degrees. Hence they cannot be recognized as distinct entities on this basis; neither can they be accepted nor rejected as neoplasms on this basis.

Encapsulation. Fetal adenoma is usually described as an encapsulated nodule.

Encapsulation. Fetal adenoma is usually described as an encapsulated nodule. It must not be forgotten, however, that in its earliest stages it is not encapsulated. In the thyroids of individuals in middle life there may be encountered minute non-encapsulated masses, the exact duplicates morphologically of what has been known since Wölfler's time as fetal adenoma. If such a lesion is a growing or quiescent embryological rest, then it is not encapsulated and yet it is generally accepted as a fetal adenoma. On the other hand, if such a lesion has developed from adult thyroid tissue, it represents complete reversion to a tissue resembling the thyroid of a fetus. In either case fetal adenoma and nodular hyperplasia are indistinguishable and encapsulation may be absent in the developmental phase of each. In the more advanced stages encapsulation may be pronounced in both the fetal adenomata and the so-called nodular hyperplasias.

If fetal adenoma is acceptable as a neoplasm on the basis of encapsulation, this is none the less true of so-called nodular hyperplasia.

Lobulation. One of the most striking and constant differences between normal thyroid tissue and nodular goiter is the absence of lobulation in the encapsulated nodules. This is quite in keeping with the characteristics of benign glandular neoplasms in other organs and tissues. That the absence of lobulation is not merely a matter of the character and degree of hyperplasia of the epithelium is indicated by the fact that even in the most extreme hyperplasia associated with exophthalmic goiter the normal lobular architecture of the gland is maintained. In the most extreme hyperplasia associated with recurrence of exophthalmic goiter after operation the normal lobular architecture is maintained, and this is also true in the hypertrophy and hyperplasia following partial ablation in animals.

So far as absence of lobulation is concerned, there is no distinction to be made between fetal adenoma and so-called nodular hyperplasia.

Departure from Normal Structure. Whatever may be urged as points of difference between so-called fetal adenoma and so-called nodular hyperplasia with reference to

origin, differentiation, functional capacity, encapsulation, lobulation, size, number, and growth, there is one point on which there is little occasion for divergent opinions, namely, *that both forms of nodular goiter exhibit increasing structural departure from normal thyroid tissue.* Our criteria for judging the degree of departure are largely if not exclusively morphological. With this crude method for measuring variations we can but admit that *with an increasing departure from normal structure there is an increasing approach to neoplasia.*

Summary. That nodular goiter has its origin in non-tumorous thyroid tissue is not of necessity an indication that it is non-neoplastic, since carcinoma and sarcoma may originate in non-tumorous parent tissue. That the nodules in the thyroid are not possessed of unlimited growth is of no greater significance than is the similar observation with reference to adenomata of the breast. That the natural tendency to display further unmistakable evidence of neoplasia (malignancy) is but relatively feeble in nodular goiter is of no greater significance than is the similar observation that fibromyomata of the uterus exhibit but a feeble tendency to unmistakable neoplasia (malignancy).

That the nodules may assume and maintain certain morphological characteristics approaching those of non-neoplastic thyroid; that they are composed of glandular structures similar to those of non-neoplastic thyroid; that these glands may contain colloid, can bind and store iodine, and have been shown to contain the active principle of the thyroid; that they can undergo hypertrophy, hyperplasia and involution comparable to similar changes in non-neoplastic thyroid; these qualities at least constitute a rather doubtful basis for excluding nodular goiters, particularly in the more advanced stages, from the category of benign neoplasms. All of the foregoing qualities are discernible in encapsulated masses in the thyroid that are unmistakably malignant, as evidenced by metastasis, invasion, destruction and death, and are therefore unquestionably neoplastic.

In view of all the foregoing considerations, it seems permissible to regard the usual arguments against the neoplastic nature of the process by which the thyroid becomes nodular as somewhat specious. Exclusion of nodular goiter, at least in the advanced stages, from the category of benign neoplasms seems a doubtful expedient, which apparently in no way clarifies clinical or pathological problems. By analogy and by the principles of general pathology, the encapsulated masses of non-lobulated thyroid tissue that do not invade, do not metastasize, and do not present histological characteristics which may be recognized as those of cancer, should be classified among the adenomata until we are sufficiently well acquainted with neoplasms from an etiological and biological standpoint to do otherwise. The burden of proof would seem to be on those who deny to the thyroid equal privileges with the breast, stomach, intestines, liver, pancreas, ovaries, uterus, kidneys, prostate, and various mucous membranes as regards the development of benign glandular neoplasms (adenomata).

CONCLUSIONS

1. The development of nodular goiter (exclusive of inflammatory nodules and malignant neoplasms) is, in all probability, dependent upon a single process or mechanism rather than upon multiple processes or mechanisms of fundamentally different character.

2. Differences in degree of reversion (de-differentiation), growth, differentiation, encapsulation, and structural departure from otherwise normal thyroid tissue offer a satisfactory explanation of the gross and microscopic variations observed in nodular goiters. Such a conception obviates the necessity of invoking an embryological defect, for which insufficient objective evidence has been adduced, to explain the so-called "fetal adenoma" of Wölfler.

3. Nodular thyroids associated with endemic goiter, hypothyroidism and hyperthyroidism are intimately related in point of origin to the hyperplastic phase of thyroid overgrowth rather than to the involutional phase. The latter may be a factor of some importance in determining the morphological character of the end result.

4. The process of nodulation may have its inception in fetal life, postnatal life, during puberty, adolescence or adult life.

5. From a morphological standpoint the end result of the process of nodulation, that is the encapsulated mass of non-lobulated thyroid tissue should be included in the category of benign glandular neoplasms.

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OXYGEN TREATMENT WITH SPECIAL REFERENCE TO TREATMENT OF COMPLICATIONS INCIDENT TO GOITER*

SAMUEL F. HAINES, M.D., AND WALTER M. BOOTHBY, M. D., F.A.C.S.

ROCHESTER, MINN.

FOLLOWING the development of a comparatively new method of treatment annual reports of progress may be of value for a few years even though new facts of importance may not have been brought out. For this reason, we are reporting further on the treatment by the administration of oxygen in closed chambers and in closed-circuit tents. Oxygen treatment received its greatest impetus from the the work of Haldane who, during the War, found that marked benefit could be obtained from its adequate administration to men who had been gassed. Subsequently, experimental data on administration of oxygen were obtained by Barcroft, Hunt, and Dufton in England, and clinical investigations were initiated by Hunt at Guy's Hospital, London. Later, clinical investigations were carried out by Campbell and Poulton, especially in cases of mild types of pulmonary disease. In America, Stadie, Binger and Barach have been pioneers in the continued development of efficient methods of administering oxygen.

Two years ago, we reported on our first year's experience with treatment in oxygen chambers that were constructed at The Mayo Clinic in 1926. Last year we reported results of such treatment of complications following thyroidectomy. In this report we shall deal with all the cases on the goiter service in which surgical treatment was given and those in which oxygen was given before the institution of surgical treatment. The complications arising in such a group of cases are frequently of such nature that oxygen would be expected to be of great benefit. In hyperthyroidism, anoxemia* seems to develop easily because of the increased oxygen consumption; experimental evidence favors this clinical observation. Asher and Duran found that rats rendered hyperthyroid by the administration of desiccated thyroid were unusually susceptible to oxygen deficiency, and Asher and Streuli found the converse true in rats whose thyroid glands had been removed.

Pulmonary edema is a common cause of anoxemia. Certain factors predisposing the patient to the development of pulmonary edema are occasionally found in cases of goiter, particularly if hyperthyroidism is present. Respiratory obstruction causes an increase in the intensity of the inspiratory effort, and is thus a frequent precursor of pulmonary edema. This mechanism has been reproduced experimentally by Auer and Gates, and by Loeb, by the intratracheal injection of epinephrine, and the subsequent development of pulmonary edema, except in those cases in which the increased negative intrapulmonary pressure was avoided by other means. Respiratory obstruction as a result of tracheal pressure, of pressure on the recurrent laryngeal nerve with resultant vocal-cord paralysis, or of excessive tracheal mucus, occurs oc-

* Anoxemia is used in the physiologic sense to indicate diminution in the oxygen pressure rather than merely the oxygen content of the blood.

* Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929. Some of the data in this paper are taken from a thesis submitted by Dr. Haines to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of Master of Science in Medicine, 1929.

casionally in the preoperative and postoperative treatment of any considerable number of patients with goiter. Another factor in the causation of pulmonary edema may be explained by Welch's old theory of acute pulmonary edema. He stated that this condition may be the result of "a disproportion between the working power of the left ventricle and of the right ventricle of such character that, the resistance remaining the same, the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." The disturbances in cardiac function so frequently found in patients with hyperthyroidism often might tend to produce pulmonary edema by this means. Another fact that may influence the reaction of any patient to any of the preceding disturbances is the varying susceptibility of different persons to oxygen deficiency. This is well illustrated in the varying tolerance of different persons to high altitudes.

Besides the foregoing causes of pulmonary edema, it is probable that anoxemia itself may be a factor in exaggerating this condition. The most significant work along this line that has come to our attention is that by Landis. He found that oxygen lack increased the permeability of the wall of the capillary, not only for fluid, but also for protein, with a reduction of the effective colloid osmotic pressure of the plasma. This change he found to be reversible. It seems reasonable, in view of these facts, to assume that decreased oxygen tension in the pulmonary alveoli, caused by respiratory obstruction of one kind or another, increases the degree of pulmonary edema and that the rapid subsidence of pulmonary edema in some cases after the institution of oxygen treatment may be the result of reversing the process. That this phenomenon may be of particular significance in the lung is suggested by the much higher oxygen tension normally present in that organ in contrast to the oxygen tension in most other tissues of the body; in this connection the experiments of Campbell are interesting; pulmonary edema developed when in his experiments rabbits were exposed to low oxygen tensions.

Bronchopneumonia, which so often follows the development of pulmonary edema, is a common cause of cyanosis, and one which figures prominently in the series of cases we have studied. The mechanism for the development of cyanosis in pneumonia may be, as Lundsgaard and Van Slyke have stated, either insufficient oxygenation of blood passing more or less aërated but edematous lung tissue, or to a fraction of blood passing through consolidated, unaërated lung tissue. In bronchopneumonia there are extensive areas of edema in the lung as well as areas of consolidation, so that it is probable that both the foregoing factors are present. It seems likely that the first factor, that is, insufficient oxygenation of blood passing through the more or less aërated edematous lung tissue, is the more significant. This may well account for the more striking results of oxygen treatment obtained in cases of bronchopneumonia than in cases of lobar pneumonia, the effect in the former cases being chiefly the result of accumulation of fluid on and within the walls of the alveoli and bronchioles, which, as Hoover and Barcroft have suggested, decreases the rapidity of diffusion of oxygen. As the blood passing through completely aërated portions without edema cannot take up an excess of oxygen, the average saturation of the blood leaving the lungs by the pulmonary vein will be reduced in proportion to the oxygen tension and quantity of blood passing through consolidated portions of lung and through the edematous parts in which the rate of oxygen diffusion is reduced.

A study of the dissociation curve of oxyhemoglobin showed that even when the blood leaves the lungs only 80 per cent saturated there is still a sufficient quantity of oxygen in the blood to meet the needs of the tissues, although the pressure at which it will be delivered is abnormally low. The difficulty is not, therefore, due to

the decrease in absolute amount of oxygen but rather to the pressure or tension at which it is delivered to the tissues. For example, if the hemoglobin is normally saturated at 97 per cent in the lungs and as it leaves the tissues is 60 per cent saturated the tension or pressure at which the oxygen is delivered will be approximately 38 mm. On the other hand, if the hemoglobin is originally only 80 per cent saturated (other factors remaining constant) the oxygen may be delivered at a pressure as low as 30 mm. Furthermore, the peculiarities of the dissociation curve of hemoglobin are such that other factors than its percentage saturation in the lungs affects the tension or pressure at which the oxygen is delivered to the tissues. One such factor is the acidity or the carbon dioxide content of the blood; if by rapid shallow breathing the arterial carbon dioxide tension is lowered from 40 to 20 mm. the tension or pressure of the oxygen as it is delivered to the tissues at 40 per cent desaturation falls from approximately 32 to 24 mm., although the quantity of oxygen utilized by the tissues will be the same, as will also the quantity still left in the hemoglobin.

Anoxemia means literally a decrease in the quantity of total oxygen in the blood. However, physiologically the meaning has been changed to indicate a decrease in the quantity of free oxygen in the plasma and this in turn is dependent on the factors which influence the dissociation curve of oxyhemoglobin, that is, the percentage saturation at a given tension. The fact to remember c early is that the administration of oxygen raises the tension at which the oxygen is delivered to the tissues but does not alter the amount used by the tissues. Conversely, the harmful effect of anoxemia is not due to the fact that the tissues do not actually get the amount of oxygen they need but that they must struggle to obtain the oxygen from an environment in which the oxygen, although delivered in ample quantity, is at very low pressure or tension.

In this brief review of the physiologic basis of oxygen treatment we have merely referred to the major points. Enough has been said, however, to show that the treatment has a sound basis and one should expect excellent results if it is utilized in suitable cases. With few exceptions we have selected for treatment patients who would theoretically be benefited thereby and in consequence they were nearly all at least slightly cyanotic or presented symptoms which would presumably lead to cyanosis if unchecked. Only occasionally have patients with other types of the disease been admitted to the chamber, largely for purposes of comparison; these have consisted of patients with exophthalmic goiter crisis, severe hyperthyroid reactions, and chronic cardiac decompensation. Although we have not as yet sufficient evidence to warrant a definite statement regarding them, we have at least not seen such strikingly beneficial effects as in those presenting evidence of anoxemia or of impending anoxemia.

Immediate evidence of benefit to the patient may be noted if the case is suitable for oxygen treatment. Cyanosis, if present, is rapidly cleared. The respiratory effort is much less. The majority of patients having respiratory difficulty voluntarily state that they are much more comfortable in the oxygen chamber. The characteristic drop in temperature, to which we have previously called attention, is an excellent indication, in most cases of the effect of oxygen. It is possible that anoxemia increases the sensitivity of the heat center in the brain to those abnormal metabolites resulting from bacterial invasion of the organism. When a patient with fully developed pneumonia is admitted to the oxygen chamber, it is usual for the course of the pneumonia, as indicated by physical signs of consolidation and ultimate resolution, to follow the usual progress of this disease, but the constitutional reaction is, as a rule, much less marked than would be anticipated. This is indicated by a lower temperature level, absence of difficult

respiration, and the patient's greater comfort. A number of patients have been admitted to the oxygen chamber following a sudden rise in fever accompanied by difficult respiration: as a rule a small area of dullness with râles was present but there were practically no changes in breath sounds. It is assumed, from the foregoing evidence, that these patients have advanced pulmonary edema or very early bronchopneumonia. In some of the cases the disease will progress to the development of frank pneumonia; in many, signs of rapid clearing in the chest will be present, with the usual rapid subsidence of fever. Whereas we realize that we have no means of predicting the outcome in such cases, we believe that the subjective and objective symptoms of the disease are less severe if treatment with oxygen is given than if it is not given.

TREATMENT IN OXYGEN CHAMBERS AND IN OXYGEN TENTS

One hundred forty-three patients suffering from goiter were treated in the oxygen chamber in the last three years. Three of these patients were admitted twice to the oxygen chamber, thus making 146 admissions. Of the 143 patients 104 lived and 39 died; the deaths include nearly all the postoperative deaths on the goiter service.

Partial thyroidectomy had been performed on 126 of the patients. Tracheotomy for suppurative thyroiditis with marked respiratory obstruction had been performed on 1 patient; femoral embolectomy had been performed on a patient with hyperfunctioning adenomatous goiter, and 15 patients were not treated surgically. Of the 104 patients who lived, 91 (88 per cent) were considered benefited by oxygen treatment. None of 8 patients admitted to the oxygen chamber directly from the operating room to prevent an anticipated reaction was listed as improved. Aside from the fall in temperature following admission the basis for the estimate of improvement rests on the clinical evidence presented in the individual case. One hundred thirty-one of the patients had fever on admission to the chamber, and of these 108 (82 per cent) showed the characteristic drop in temperature; the average drop for the group was 2.2° in the first twelve hours in the chamber. Of the 104 living patients, 93 (89 per cent) experienced a rise in temperature after removal from the chamber; the rise averaged 1.5° in the first twelve hours. There can be no doubt but that in general these changes in temperature are the result of the influence of the oxygen treatment.

In 96 of the 146 admissions for treatment definite cyanosis was present. We have not made use of gas analysis of the blood in our clinical work as we consider it not only unessential but impracticable for the determination as a routine of the indications for oxygen treatment. Stadie has shown that 10 per cent oxygen desaturation of the blood will be manifested by visible cyanosis. It is, therefore, probable that in some of the cases in which there was no cyanosis at the time of admission, the oxygen tension in the tissues was below normal although not sufficiently so to cause recognizable cyanosis. Eighty-five of the cyanosed patients were considered benefited, and 11 were not benefited. Of the patients not cyanosed, 28 appeared to be benefited, and 22 were not benefited. Most of the patients who were not cyanosed and were improved by oxygen treatment had pulmonary edema, pneumonia, or respiratory obstruction, all conditions in which further progress of the disease would presumably have produced anoxemia. The average drop in temperature in the first twelve hours was 2.1° in the patients showing cyanosis and 1.2° in the patients who were not cyanosed. In the latter group the temperature dropped considerably in a few instances; this was seen chiefly in cases of pulmonary edema, pneumonia, or respiratory obstruction. It is thus apparent that a high percentage of patients with cyanosis will be benefited by oxygen treatment, and that patients with conditions presaging the development of cya-

nosis are so frequently benefited that they should also be given advantage of such treatment.

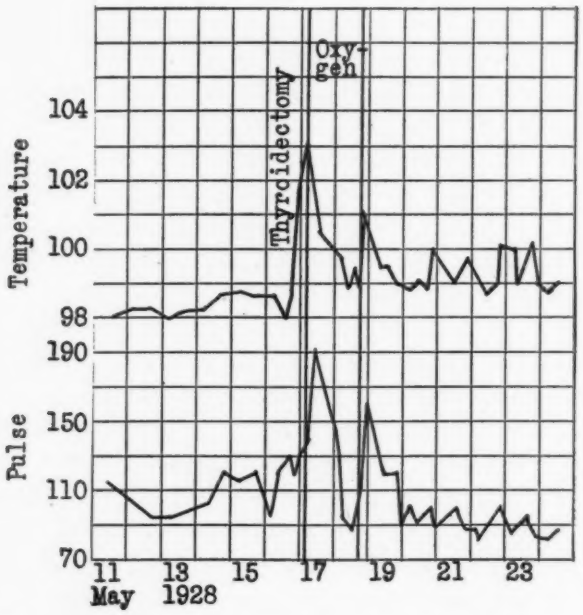

FIG. 1. Sharp drop in temperature after administration of oxygen was begun and rise in temperature after its discontinuance may be noted.

Twenty-nine patients in the series were treated in oxygen tents. These patients needed oxygen treatment at times when both chambers were occupied. Ten of the patients were moved from the tent to the oxygen chamber when one became available. Twenty of these patients had exophthalmic goiter, 7 hyperfunctioning adenomatous goiter, and 2 carcinoma of the thyroid gland. Twenty-eight of the patients had had thyroidectomy, and 1 had had hysterectomy after the control of recurrent exophthalmic goiter by iodine. The average drop in temperature in the first twelve hours after admission to the tent was 1.4°, and the average rise in temperature in the first twelve hours out of the tent was 0.7°. Seventeen (65 per cent) of the 26 patients with fever had a drop in temperature after the institution of treatment. Of the 15 patients who were cyanotic on admission, 10 were benefited, and 5 were not. Of the 14 patients who were not cyanotic, 9 were benefited.

Thus it is seen that the results of treatment in the oxygen tent were not so strikingly good as in the oxygen chamber. A direct comparison shows the average drop in temperature in the chamber to be 2.2° and in the tent 1.4°. The average rise in temperature after removal from the chamber was 1.5° in the first twelve hours, and from the tent 0.7°. However, 19 (76 per cent) of the 25 patients who were living and were treated in tents were benefited, and 88 per cent of those treated in the oxygen chambers were benefited. Ten of the patients who were treated first in the oxygen tent and later in the oxygen chamber had an average drop in temperature of 1.1° in the tent, and subsequently 2.7° in the first twelve hours in the chamber. Usually the patient was obviously more comfortable and derived more benefit in the chamber than in the tent. This difference is probably more marked in this series of cases than it would be in a series of general surgical cases. Wilder, Binger, Judd and Moore have previously reported a large series of general surgical cases in which the patients treated in the oxygen tent were markedly benefited. Many of our patients so treated were very restless and most of them needed a considerable amount of nursing. Thus it was difficult in many cases to maintain enough oxygen in the tent, since with the nurse in attendance it was not possible to administer the oxygen continuously. If patients are not especially restless and do not require so much personal attention, very efficient treatment may be carried out in the tent. There is, of course, greater necessity for technical assistance and frequent analysis of oxygen in the tent than in the chamber.

Of the 15 patients who had not had previous surgical treatment, 10 suffered from hyperthyroidism and severe cardiac decompensation, 3 from hyperthyroidism and pneumonia, 1 from exophthalmic goiter with acute laryngitis, accompanied by edema and respiratory obstruction, and 1 was in the gastrointestinal crisis of exophthalmic goiter. Two of the 3 patients with pneumonia were benefited. Only 4

of the 10 patients with cardiac decompensation were benefited. Other treatment was instituted simultaneously in all cases of cardiac decompensation, so that the effect of oxygen itself cannot be definitely determined. In this group, cyanosis was not so common as in the other cases, as would be anticipated from their general character, and the results for the group are not strikingly good, although a few were apparently improved (Fig. 1).

SUMMARY

We believe that the therapeutic administration of oxygen by means of the chamber or tent is most helpful in a restricted group of cases, such as postoperative pulmonary edema, bronchopneumonia, and respiratory obstruction. The patients who show most marked benefit are those with evidence of anoxemia, or of impending anoxemia. Treatment should be begun as early as is possible, as in many instances the progress of pulmonary edema to pneumonia probably can be averted. Treatment should be continuous, or as nearly continuous as possible, until the pathologic process is well controlled. Binger and others have called attention to the deleterious effects of oxygen concentrations of 70 per cent or more. We have not raised the oxygen above 60 per cent for more than a few hours at a time. From these concentrations we have not seen harmful effect. Treatment with oxygen can be carried out more efficiently in oxygen chambers than in oxygen tents, although excellent results can be obtained in tents properly manipulated. We do not know that the life of any individual patient has been saved by oxygen treatment; however, we believe that at least an occasional patient is saved when marked lowering of the temperature and increased comfort can be secured in such a large series of patients who are seriously ill. Our results not only warrant the continuation of this method of treatment but indicate the advisability of more general adoption of efficient methods of the administration of oxygen in those diseases known to be benefited by its use. The patients who obtain the greatest benefit are those with postoperative pulmonary edema, bronchopneumonia, or respiratory obstruction accompanied by cyanosis or impending cyanosis.

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IS GOITER ENDEMIC IN SOUTH CAROLINA?*

JAMES A. HAYNE, M.D.

COLUMBIA, S. C.

ENDEMIC goiter has been supposed to be practically unknown in South Carolina, although the only basis for such a view is in the analyses of draft board statistics made by Dr. Robert Olesen and the observations of pediatricians within the state. The studies of McCendon on water supplies have added weight to the iodine deficiency theory, and yet no natural waters in the United States, with the exception of a few highly mineralized wells and springs, contain sufficient iodine to provide for normal needs, even on the basis of the extremely low daily requirement assigned by Fellenberg.

South Carolina is hence a very good field for the study of iodine in human environment. Many analyses of vegetable foods have been made by Dr. Roe E. Remington in the food research laboratory at the State Medical College at Charleston, the very striking results of which are shown in Table I, in which are also included analyses of products from other localities by McClendon. In this table, the iodine content of some South Carolina vegetables is compared with results published by Dr. McClendon for vegetables produced in California and Oregon. Results are in parts per billion of iodine in the dried vegetable.

TABLE I

Vegetable (Dried)	Iodine (Parts per Billion)		
	South Carolina	California	Oregon
	Analyses by Remington	Analyses by McClendon	Analyses by McClendon
String Beans	429	....	29
Beets	233	8.0	....
Carrots	135	8.5	2.3
Lettuce	754	....	....
Peaches	192	....	11.1
Peas	197 (ripe)	8.4 (green)	....
Potatoes	517	....	....
Spinach	424	26.0	19.5
Soup Vegetables	....	....	13.5
Squash	1018	....	....
Sweet Potatoes	135	....	....
Tomatoes	273	17.5	....
Asparagus	112	12.0	....

It has been found that the green leafy vegetables such as spinach, lettuce, kale, etc. (which incidentally have also been shown to be rich in vitamines and iron) are the best natural sources of iodine we have, and that second to these come roots such as beets, carrots, potatoes, etc. Grain from South Carolina, as elsewhere, is a poor source of iodine.

As a basis for comparing the iodine content in different parts of the state, 69 samples of Irish potatoes have been collected, examined, and the results tabulated. It was found that the values could vary over several hundred per cent in the same locality, without any cause being clearly evident. Such being the case, it seems risky to generalize from as few as 69 samples, but lines were drawn across the map at fifty-mile intervals from the coast, and the samples from each fifty-mile belt averaged as shown in Table II.

TABLE II

IODINE CONTENT OF POTATOES IN RELATION TO DISTANCE FROM THE SEA

(Parts per Billion, Dry Basis)

Distance from Sea, Miles	Number of Samples	Iodine Content (Average)
0– 50	19	180
50–100	16	213
100–150	15	223
150–200	15	249
Over 200	4	266

* Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929.

At least so far as this study goes, the salt spray theory cannot explain the distribution of iodine in the agriculture of our state. Mitchell, of Clemson College, has examined the surface waters of the state, finding the greatest amount of iodine (6 parts per billion) in the Broad River at a point some 150 miles from the coast. Furthermore, this is about 25 per cent of the concentration of iodine in the Atlantic Ocean, and could not possibly have been all derived from sea spray. The Broad River is not brackish.

TABLE III

IODINE CONTENT OF POTATOES IN RELATION TO SOIL AREAS

(Parts per Billion, Dry Basis)

Soil Area	No. of Samples	Iodine Content (Average)
Coastal Region.....	7	198
Lower Pine Belt.....	16	164
Upper Pine Belt.....	12	234
Sand Hills.....	7	191
Piedmont.....	27	249

An attempt has also been made to correlate iodine values with soil types. South Carolina is roughly divided in half by the "fall line," below which the soils are sand or sandy loam and have come up out of the sea in comparatively recent geologic times. Above the fall line the predominating type is a red clay or clay loam, brought down by erosion from the granite rocks of the Appalachian System. Average values for the different soil types are given in Table III.

It will be noted that the samples from the Piedmont, above the fall line, are richer in iodine than those from any of the lower areas, not excepting the coast itself.

Our country health officers in about twenty counties have examined 20,000 high school students for thyroid enlargement. The amount found is considerably lower than in any region where similar surveys have been made, excepting possibly the coastal part of Connecticut, and it is equally interesting that Columbia (in the sand hills) shows more goiter than either Charleston (on the coast), or Greenville (in the Piedmont). We are inclining towards the idea that vegetable food raised in a region where iodine is available in the soil is the normal and natural source of iodine for human beings.

LATE CARDIAC MANIFESTATIONS OF TOXIC GOITER*

C. B. LUGINBUHL, M.D.

DES MOINES, IOWA

THE association of thyroid disease and heart changes was pointed out by Adelmann in 1828, and in the latter half of the century that has since elapsed considerable study has been devoted to the goiter heart. Yet in spite of the clinical and experimental work that has since been done, the essential differences between functional, and organic cardiac manifestations occurring incidentally during the course of thyroid disease and such symptoms developing as the result of toxic goiter, apparently still fail of appreciation and correct evaluation. Yet the fate of the goiter patient is so intimately linked with the condition of his heart muscle that a clear understanding of the clinical and pathological heart picture and its therapeutic and prognostic significance are essential if optimum results are to be achieved in our treatment of the goiter patient.

The characteristic over-demonstrative heart of the thyrotoxic patient must be mentioned here for the purpose of elimination. It is the most constant symptom of thyroid disease, and the exaggerated response of such a heart to even casual stimuli is an early and generally recognized symptom of thyrotoxicosis. It may persist for an indefinite period, for many years, in fact, only to disappear without leaving demonstrable evidence of organic damage, once the toxic stimulus is eliminated. The severity of the heart symptoms, of which the patient himself is often painfully conscious, and the absence of demonstrable organic lesions are at striking variance.

In the typical goiter heart, however, we are dealing with an accomplished fact and not with a potential one. From the standpoint of therapy as well as of prognosis it is the condition of the heart that assumes major importance: first, whether the heart lesion is of primary development and the development of a goiter a coincidence; second, whether the heart lesion is a chance development in a patient already afflicted with goiter; or, third, whether the heart lesion is secondary to thyroid disease. The treatment of a goiter patient is always an individual problem, and this is particularly true of the goiter patient with heart disease, yet from the standpoint of etiology of the heart symptoms we must distinguish three general groups: that of mechanical origin, that of toxic origin, and that in which both mechanical and toxic factors have had a part.

In the European countries where goiter is endemic mechanical goiter heart is said to be the most frequent cause of secondary heart disease, but in America such origin is the exception and not the rule. Moreover, in these so-called goiter regions, the mechanical goiter heart is usually found in patients afflicted with massive colloid goiters, while in this country it is the adenoma of the thyroid, often the adenoma of moderate size but of strategic location, which is incriminated. The mechanical goiter heart does not come within the scope of this paper except where the toxic as well as the mechanical factor enters in, as has been the case with a majority of our patients.

Rose's theory of the development of the mechanical goiter heart, though not uncontested, is probably the most generally accepted. Rose held that the heart changes are secondary to degeneration of the trachea resulting from its compression by the enlarged thyroid; the tracheal malacia interferes with respiration, particularly with inspiration, and through obstruction

* Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929.

of the lesser circulation leads to capillary atrophy; the circulatory changes in turn impose an overburden on the right heart, manifest in time as hypertrophy of the right ventricle. Sulger has recently brought experimental evidence in support of this explanation; he succeeded in producing an enlargement of the heart by obstructing inspiration by means of compression of the trachea; interference with expiration alone resulted in a decreased rather than an increased heart volume.

Clinical evidence which the surgeon sometimes records with regret is found in the alarming and even disastrous interference with heart function when a postoperative hematoma compresses the trachea. In 2 of our cases in which the mechanical factor was particularly clear, partially calcified adenomas of the thyroid compressed the trachea on deep inspiration so that Bryson's sign was a striking symptom, the patients even struggling from their beds when an unusually deep inspiration brought on a typical attack of dyspnea. The fluoroscope and roentgen ray are of value in detecting changes in the size and shape of the heart as well as deformities of the trachea. Basal metabolic rate readings are always of interest, but the fact that there may be only a moderate increase in rate or even no increase does not necessarily eliminate the toxic equation.

The effect of hyperfunction or of dysfunction of the thyroid upon the heart is generally accepted, but the direct cause of these cardiac changes is still a subject for debate. While it is often held that the burden imposed upon the heart by persistent tachycardia is alone responsible for the development of dilatation, hypertrophy, and myocardial degeneration, there is abundant clinical evidence that the heart may meet the increased functional demands imposed upon it by tachycardia over a period of years, and once the tachycardia is relieved, there may be no demonstrable evidence of organic change. A specific effect of thyrotoxin upon the heart muscle has been assumed, and recent experimental work by Takane is of considerable interest. Takane found that of every patient dying of Basedow's disease the heart evidenced chronic inflammatory changes or a diffuse leucocytic infiltration in addition to an accumulation of lymphocytes. Fahr, reporting the histological examination of 5 goiter hearts, found in 2 interstitial myocarditis with leucocytic infiltration, fibro-blasts between the muscle fibers in the region of the blood vessels, and muscle degeneration; and in 2 he noted leucocytic infiltration with irregularly distributed lymphocytes. Takane, by the administration of organic or of inorganic iodine compounds, was able to produce pathological changes in the heart similar to those he had observed at autopsy. Like changes were not demonstrable in other viscera, and he concluded that acute myocarditis resulted from the administration of iodine compounds because these compounds were disintegrated by lactic acid in the heart muscle. The free iodine irritates the heart since the myocardium possesses little lactate or protein to combine with the lactic acid in the heart muscle. In the liver and other parenchymatous tissues, lactic acid is also formed, but here no inflammation results since the iodine combines with the large quantities of protein present in these tissues. While these observations apply particularly to the more acute forms of goiter, there seem to be valid reasons for assuming that the same explanation would apply to those types of goiter in which the hyperfunction or dysfunction has been active for years rather than for months.

The patients in the toxic group are for the most part middle aged or elderly, and, in contrast to the group in which obstruction to respiration has played a part, women greatly outnumber men. The goiter has usually been present for years, but often it has increased in size so slowly that it has been disregarded. The cardiac symptoms as well as the symptoms more characteristic of thyrotoxicosis have been of gradual, even insidious onset, though

they may first have attracted attention following some acute illness (influenza is often incriminated) or a period of nervous stress and strain. Arrhythmias are very common. Auricular fibrillation has so frequently been noted in these patients that its occurrence calls for the elimination of thyroid disease as a possible cause. Decompensation of varying degree is common in advanced cases, and may be the symptom that brings the patient to the physician. It is thirty years since Kraus described the type of goiter heart which bears his name, yet goiter heart developing in a patient who has long had a so-called silent goiter, or who has a hyperfunctioning rather than a grossly enlarged thyroid is overlooked by many, even by most physicians.

The basal metabolic rate varies widely in the toxic group. While readings of +75 and +90 have not been rare, the rate is often only slightly or not at all increased. Determination of the size of the heart in goiter on the basis of clinical observation alone is notoriously difficult. The over-demonstrative heart is prone to give the impression of increased size, yet in those cases in which death supervenes and an autopsy is performed, the heart may be entirely normal in size and weight. Even roentgen study of the heart does not eliminate the possibility of error, since a distended heart may give the impression of a dilated or hypertrophied one. In goiter heart, however, developed through years of thyroid intoxication, demonstrable changes in volume and contour are not rare. Here the left heart is found enlarged, while in goiter heart of mechanical origin, the auricles and right ventricle are enlarged, and in the combined type, the entire heart may evidence an increase in size.

In the toxic group, a relatively large number of patients have hypertension of varying degree. I have not been able to convince myself, however, that the hypertension and the diseased thyroid and goiter heart necessarily, or even probably, bear a cause-and-effect relationship to each other. As emphasized by Loeper and Mougeot, the heart lesion may be absolutely independent of a coexisting goiter, and this observation applies with equal force to hypertension. Patients with goiter heart and hypertension are for the most part in or beyond middle life, i.e. in an age group in which arteriosclerotic changes are common. Moreover, it is not improbable that a common etiologic factor may have determined the development of both conditions, though degenerative vascular changes may be more marked in the thyroid vessels. From the standpoint of treatment and prognosis, determination of the relative importance of the rôle of thyroid and of vascular disease is of great importance. Some of the so-called goiter deaths following operation are in reality heart deaths, pure and simple; a coronary accident is a coronary accident though it occur in a goiter patient. Very recently a goiter patient who had seemed a fair surgical risk but who following some weeks of preparation seemed destined to come safely through, developed symptoms of coronary thrombosis immediately after operation. He rallied, but twenty-four hours later had a second, more severe attack to which he succumbed.

In any consideration of the treatment of the goiter patient with a heart lesion, the point which cannot be overemphasized is individualization. The advisability of surgical treatment is beyond question where an etiological relationship between heart lesion and goiter has been established. Exception must be made for one group of patients only, those whom we can only watch die. For the others, surgery holds their one hope of improvement, and he who would treat them medically assumes a burden of responsibility which he should find difficult to carry. Beside the over-optimistic or over-timorous internist we must arraign the over-zealous surgeon who rushes these patients to the operating table with insufficient preparation. Between these two, the choice depends upon personal preference for a lingering or for

an early death. Every goiter patient, and particularly every cardiac patient, should be under the observation and direction of a competent internist, not because these patients are medical but because they are surgical, when medical treatment has made surgery relatively safe, and only then.

I know of but one therapeutic measure which is of universal application to the goiter patient with a heart lesion; this is bed rest. Putting the patient to bed is unfortunately not always equivalent to securing rest in bed for him. A sedative or hypnotic is often required to quiet him and assure him the restful nights which are so essential and which he has often not known for many months. Morphine is objectionable where the sedative effect alone is required, but it may be of service in congestive heart failure where rest is imperative. Some member of the barbital group is efficient; my own choice is luminal, sometimes diallyl barbiturate. A 1 grain dose is given in the morning, say at 8:00, and 1½ grains in the late afternoon. The period of bed rest required will vary from days to many weeks, but some period of hospitalization is always essential. In auricular fibrillation or congestive heart failure, a preliminary period of rest and treatment should be followed by a therapeutic test of exertion. The patient may be allowed up and about the hospital, or may even be allowed to return home to a carefully restricted life. If he cannot tolerate such restricted activity without a recurrence of his heart symptoms, he cannot be considered a safe surgical risk. This simple effort test of cardiac efficiency is, I believe, at least as accurate as the electrocardiogram, and it has an added virtue: it is always available even at a distance from centers of population where such equipment is not always at command.

Lugol's solution is not here the worker of miracles that it is in hyperplastic goiter, but it is effective in a fair proportion of patients, and so merits a carefully controlled trial in every case. Its period of greatest efficiency is reached within a comparatively short time, and it is often most ungracious about giving an encore, so that the time of its administration deserves special consideration in order that its maximum effect may coincide with the anticipated time of operation.

The response to digitalis may also seem erratic. In the presence of a decompensation which might be expected to respond to this remedy, it may prove useless, while in a second case the response may be most gratifying. Careful inquiry may give basis for the assumption that in the latter case we are dealing with an old or coincidental heart lesion in a goiter patient, while in the former we have a decompensating toxic goiter heart, and the goiter heart is often not amenable to digitalis therapy. In the presence of auricular fibrillation, quinidine is frequently efficient, and when first given in small doses, should not give rise to disquieting symptoms. It is reputed unsafe, but in our hands has never given rise to dangerous symptoms in the treatment of several hundred patients.

The prognosis as to the future of these cardiac patients is, of course, guarded. With judgment and care, the operative mortality will be low, but the extent to which the individual heart will "come back" following operation cannot be accurately foretold. Immediately following operation, there is often a recurrence of the acute symptoms which had subsided under treatment. When this period of storm and stress has been weathered, the heart symptoms may miraculously subside, but more often improvement is slow, and is in large measure dependent upon the patient's willingness to live within his physical resources. Often the clinical improvement is more marked than is improvement in objective symptoms. The patient may consider himself cured though objectively little improvement is to be noted in his condition.

Note: For conclusions of article see author's reprints.

ANESTHETICS IN RELATION TO GOITER*

E. I. McKesson, M.D.

TOLEDO, OHIO

INSTABILITY of the nervous and cardiovascular systems in hyperthyroidism is usually the most important factor influencing the selection of the anesthetic. But its administration is as important as the kind of anesthetic employed.

Since simple goiter presents no problems peculiar to it, outside of respiratory obstruction, the following remarks are directed to the toxic cases.

SELECTION OF ANESTHETIC

The best anesthetic for thyroid operations should embody the following characteristics:

1. Ease and celerity of induction from the patient's standpoint.
2. Flexibility as well as practicability of maintaining a really light narcosis.
3. Protection from shock without producing nervous and circulatory exhaustion or depression.
4. Mechanical assistance to respiration by means of pressure in cases of respiratory obstruction and embarrassment.
5. Prompt elimination with the least possible postoperative nausea, vomiting, and restlessness.

The toxic thyroid patient is about the most unstable which the anesthetist meets. The degree of intoxication varies tremendously and requires special attention both before and during narcosis. Some improvements in preparation for operation have decreased the hazard in recent years. Extreme cases, however, are still met only too frequently, taxing the skill and judgment of both surgeon and anesthetist.

No potent anesthetic in common use is free from danger of depression *per se*. Technique of administration and constant watchfulness of the pulse, respiration and blood pressure for evidences of depression are essential for the best results. Differences in the skill of administration will always affect differences of opinion with regard to the kind of anesthetic giving the best results. Our conclusions are necessarily formed from a comparison of various anesthetics administered under similar conditions and observations.

Ether. Although ether is not as generally employed in these cases as formerly, it may be well to review its effects in the hyperthyroid case. It is an unpleasant anesthetic for the patient. Slow induction and its accumulative effects are noteworthy objections. It is rather inflexible, that is, one is often compelled to maintain a narcosis which is too deep for the well-being of these cases, in order that vomiting during the operation may be avoided. While it protects well from traumatic shock, it adds a form of toxemia and circulatory depression out of proportion to its protection. Its elimination is very slow and accompanied by nausea and vomiting which greatly interferes with the physical and mental rest these cases require for convalescence. It embarrasses respiration by an accumulation of more or less mucus. The resulting asphyxia (usually without cyanosis) often increases the blood pressure and pulse rate to a marked degree. This adds labor and exhaustion to the damaged cardiovascular system. Respiratory obstruction is not as readily controlled under ether as under ethylene or nitrous oxide with pressure because of the usual lack of proper apparatus for this purpose.

Ethylene-oxygen. Ethylene-oxygen from the standpoint of odor is unpleasant but it induces anesthesia quickly and usually without struggling. Resembling ether it requires fairly deep narcosis to prevent vomiting. Better than ether it rarely induces bronchorrhea to obstruct

* Read at the Annual Meeting of American Association for the Study of Goiter, Dayton, March 25–27, 1929.

respiration. But ethylene markedly lessens the depth of breathing which is probably responsible for the frequent increase in blood pressure from asphyxia with or without cyanosis.

Increased pulse rate and blood pressures are to be avoided as far as possible in these cases. On the other hand lowering of blood pressure to a marked extent is also undesirable. The level of anesthesia may produce first one and then the other of these conditions in the same patient.

Nitrous Oxide-oxygen. Under proper administration nitrous oxide-oxygen more nearly approaches the ideal anesthetic for the toxic goiter case.

Unlike ether or ethylene, nausea and vomiting during narcosis are rarely produced except in very deep anesthesia. Therefore, one is able in practice to maintain as light anesthesia as required without this complication. This affords the anesthetist full control of the depth of narcosis.

It is free from unpleasant odor, produces a quick induction without excitement and never, in itself, produces bronchorrhea. It does not restrict the tidal respiration by central depression, except in very deep narcosis which should not be employed, and usually does not increase blood pressure when properly administered through the aid and control of blood-pressure determinations. The toxic goiter case is prone to circulatory depression as a result of deep anesthesia. On the other hand, if anesthesia is conducted so light as to result in active reflexes, the pulse rate, respiration and blood pressure may be increased, which in the more toxic cases may lead to early exhaustion or shock. Nitrous oxide is rapidly eliminated and does not cause protracted nausea and vomiting.

HYPNOTICS

In the writer's opinion, morphine dosage is a very important factor in technique. In normal cases the metabolic rate is decreased about ten per cent per ¼ grain of morphine (without atropine). Owing to the irritability of hyperthyroid cases one dose of hyoscine gr. $\frac{1}{100}$ is preferable to atropine. Subsequent doses of morphine alone are administered in doses varying from ⅛ to ¼ gr. or even more depending upon the degree of toxicity or effects on the patient. Enough should be administered to reduce excitability before and pain after the operation. It is not always possible to secure definite drowsiness. Under these conditions it is never necessary to maintain deep nitrous oxide-oxygen narcosis nor to induce either central or peripheral asphyxia as evidenced by cyanosis, unless there is respiratory obstruction as a complication.

BLOOD-PRESSURE REACTIONS

The sphygmomanometer is, in fact, an essential instrument in the proper control and administration of an anestnetic in these cases. Without it, one unconsciously maintains narcosis on an improper plane, usually too deep, but sometimes also too light.

Hyperthyroidism exaggerates the normal responses to anesthetics as it exaggerates normal psychic reactions in the conscious patient. High blood pressures and pulse rates may be increased or decreased in two dual sets of reactions: (1) A slow induction of narcosis usually increases pulse and blood pressure, but as light anesthesia with unconsciousness and loss of reflexes approaches these fall either to the patient's normal or slightly above or below. (2) Under deeper anesthesia blood pressure may either *rise* with or without an increased pulse rate, depending somewhat upon the central effects; or the pressures may *fall* either slowly or abruptly depending upon the depth of anesthesia. In this phase one may also observe a transient rise in pulse rate before it falls to a considerable extent.

It is the duty of the anesthetist so to regulate hypnotics and the depth of narcosis as to avoid large fluctuations of the pulse, respiration and blood pressure, recording these functions every few minutes upon a suitable graphic chart, so that

the tendencies toward depression may be obvious by glancing at this chart.

DEPRESSION TEST

Very gradual insidious development of depressions in these cases from unsuspected deep narcoses are so common that either a marked rise or fall in blood pressure is the signal to make a depression test to determine whether or not the anesthetist is in error in his administration. The test is performed as follows: After taking and recording both the pulse rate and blood pressure, the pressure in the cuff is held at the systolic pressure while from 1 to 2 breaths of a mixture of ethylene or nitrous oxide-containing considerably more *oxygen* than had been used, are now inhaled. The average increase of oxygen for this purpose is 25 per cent. After these inhalations, the old mixture is restored, while one follows the upward or downward course of the systolic pressure during the next minute or two by either inflating or deflating the cuff as the blood pressure changes.

This depression test is applicable in any operation, but is often more pronounced in its reaction in hyperthyroid cases than in most other conditions. It is not very uncommon to see the systolic pressure temporarily rise from 80 to more than 200 mm. Hg. within one minute after the addition of oxygen or to fall from 200 mm. to the patient's previous normal in the same period of time.

With such a positive reaction to this therapeutic test, it is readily shown that the patient was being relatively overdosed and depressed, and a new mixture is sought to restore a more normal state of pulse and blood-pressure ratios. It should be said that a positive depression test is sometimes also indicated by either a rise in pulse rate if it has been slower than usual or a fall in rate when it was more rapid than usual.

Now in searching for the proper anesthetic mixture, care is necessary to avoid active reflexes of pain from light anesthesia and also to avoid abrupt large changes in the level of narcosis. Local anesthesia would seem a logical aid but we find it unnecessary. Once marked depression has

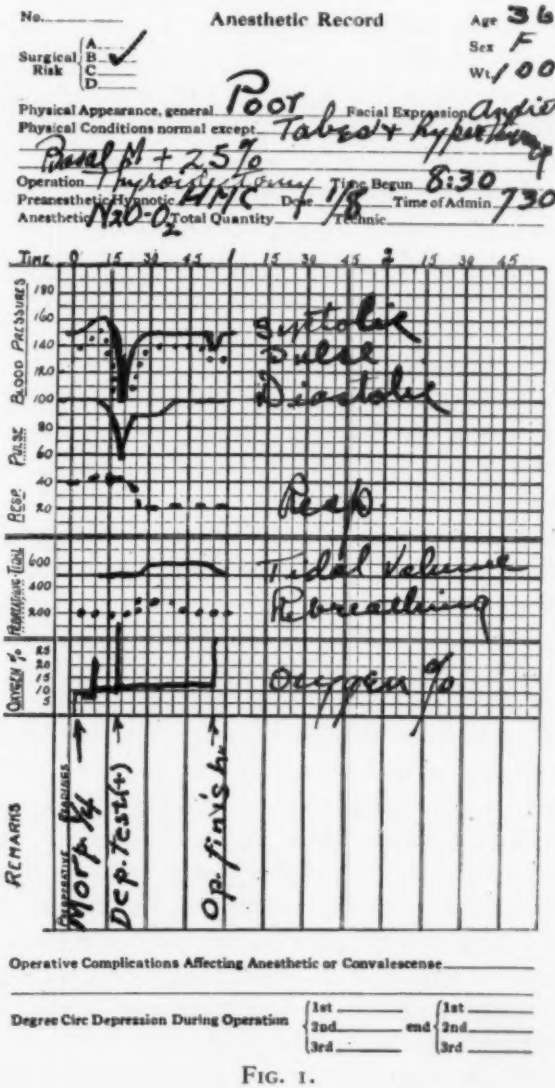

Fig. 1.

been permitted to develop, the patient tends to relapse into another and another until normal relations of these functions cannot be reestablished, unless great skill is exercised in the further management of the anesthetic. Time is an important factor. Prolonged operations under these conditions increase the hazard to a marked degree. The rapid operator probably avoids some of the complications, particularly if the anesthetist is equally dexterous and watchful in detecting early signs of depression and in correcting his mixture accordingly.

A negative response to oxygen with depression progressing is a warning worthy of immediate consideration by the surgeon.

The usual signs of anesthesia are not sufficient for the anesthetist. He must take the blood pressure to perform his best services. Without any other warning with which the writer is familiar, may the gradual insidious circulatory depression be detected until so far advanced that the reestablishment of normal relations, particularly in hyperthyroid cases, is almost impossible to maintain.

RESPIRATORY OBSTRUCTIONS

From pressure of the tumor upon the trachea, the airway may be partially obstructed before operation and exaggerated *during* the liberation of the gland. Kinks, torsion, ligatures, sutures, and perforations of the trachea may complicate the anesthetic and operation in certain cases. The anesthetist must be prepared to cope with such situations promptly and effectively.

Inspiration is always the phase of respiration requiring assistance. If air can be gotten into the lung, the patient will force it out. When obstructive breathing is encountered, the anesthetic should be administered under enough pressure to assist in filling the lungs. Properly designed gas-oxygen apparatus makes this not only possible, but easily accomplished without tracheotomy.

While obstruction to respiration may be acute, which is immediately corrected by manipulation or the removal of ligature or suture, the more dangerous types are those in which freedom of airway is just slightly inadequate at the time to become acute some hours later after swelling has occurred. Here again the anesthetist should be on guard by actually *measuring* the tidal respiration to determine whether or not the patient *without* the aid of pressure is able to inspire at least 8 liters of gas per minute without evidences of embarrassment or effort.

When the patient shows effort in breathing 6 liters per minute an acute obstruction may develop later on as shown in one of the writer's cases. Under pressure, these cases may be resuscitated with oxygen, reanesthetized, the wound reopened and the obstruction relieved without a tracheotomy.

CONCLUSIONS

1. Light anesthesia properly maintained is needed in toxic cases.

2. Nitrous oxide-oxygen anesthesia is best suited for these cases since nausea and vomiting do not result from light anesthesia as in other anesthetics, and the proper plane of anesthesia is always obtainable. .

3. The anesthetic should be checked by means of blood-pressure determinations to detect depression as a result of improper narcosis.

4. Narcosis under pressure when respiratory obstruction is encountered is conveniently applied and is efficient in relieving it during operation, avoiding recourse to tracheotomy.

PARATHYROID PROTECTION*

H. H. SEARLS, M.D.

SAN FRANCISCO

POSTOPERATIVE tetany, described first by Weiss in 1881, was then thought to be a part of the picture of postoperative myxedema. Ten years later, however, Gley in a series of experiments on animals offered conclusive evidence to prove that the development of tetany was due to the removal of the parathyroid glands.

Halsted was greatly interested in the parathyroids and their protection. Under his direction Evans in 1907 carefully worked out their anatomy, demonstrating particularly that their main blood supply came from the inferior thyroid arteries, and that they usually lay directly on the posterior capsule of the thyroid gland. From these observations ligation of the inferior arteries would seem hazardous because of the possibility of thereby limiting the blood supply to the parathyroids.

MacCallum and others showed that associated with tetania thyreopriva there was a lowered calcium content in the blood. The administration of calcium by mouth or intravenously was found to be of extreme benefit to the tetanic patient.

Recently Collip has isolated an active principle, parathormone, from the parathyroid gland which when injected into an animal causes a rise in the blood calcium. In parathyroidectomized animals a normal blood calcium, a hypocalcemia or a hypercalcemia can be effected at will by administering graded amounts of parathormone, the blood calcium content varying directly with the dosage. Both hypercalcemia and hypocalcemia cause alarming symptoms but it is the latter condition which is of chief interest to the surgeon.

The clinical picture associated with parathyroid insufficiency is as disconcerting to the thyroid surgeon as to his luckless patient. In the advanced state such insufficiency is fortunately rare, but evidence of slighter disturbances of parathyroid function, if carefully looked for, may be fairly frequently demonstrated in the postoperative course of goiter patients. The routine employment of the Chvostek, Trousseau and Erb tests, by demonstrating the characteristic increased irritability of motor nerves, aid in the detection of the mild or subtetanic cases. Blood calcium determinations offer a further check on the condition.

Parathyroid insufficiency severe enough to cause tetanic convulsions is rare, but one case with this complication will suffice the surgeon for a lifetime and give to him a tremendous stimulus for the development of a technique insuring parathyroid protection.

The parathyroid glands, usually four in number in the human, are small, oval, flattened, yellowish or brownish bodies averaging about 4 by 3 by 2 mm. in their dimensions. They are most commonly found in the loose areolar tissue on the external surface of the posterior portion of the thyroid capsule in the so-called "channel of anastomosis" between the posterior branches of the inferior and superior thyroid arteries. Quite frequently, however, they lie farther around on the lateral or even the anterior capsule. Their appearance and location make their identification fairly simple. A relatively large unbranched parathyroid artery may always be demonstrated entering the hilus of the glandule. They are perhaps most commonly confused with small lymph nodes or hemolymph nodes but these latter lack the yellow tint and are of firmer consistency. Under the microscope the characteristic cells and pattern of the ductless gland type are easily recognized by the trained histologist (Fig. 1). Relatively large amounts of fat are often contained within the gland capsule and scattered between the cells, thereby causing a characteristic yellowish color. The gland cells are arranged in irregular groups and cords

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and occasionally in alveolar patterns. From the connective-tissue capsule fibrous septa penetrate into the gland substance. Numer-

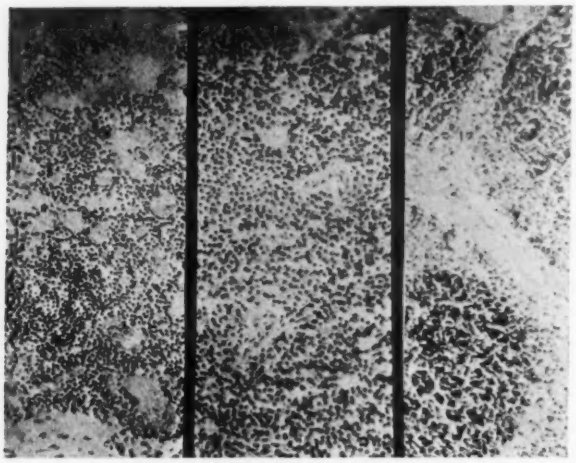

Fig. 1.

ous large thin-walled blood vessels surrounded by only a small amount of fibrous tissue run through the parenchyma. All parathyroids reported in this series have been checked by microscopic examination (Figs. 2 and 3).

The development of severe tetany in one of my patients coupled with the subsequent identification of three parathyroids on the lateral and anterior capsules of the specimen removed in this case caused us to accept at once Lahey's plan for immediate search of removed specimens for any parathyroid tissue and for its reimplantation if found. In thus examining specimens for the glandules it was noted that they were always associated with the thyroid capsule and were most frequently found well forward on the lateral surface of the thyroid lobes and occasionally even on the anterior capsule.

Where the anterior branches of the inferior thyroid arteries curve up over the lateral capsule at the inferior poles of the removed lobes, parathyroids are most often demonstrated. These areas are true danger zones to be avoided and not removed. It is interesting that Dr. Halsted in 1907 advised the preservation of somewhat similar areas at the lower poles. He had noted fewer cases of tetany where such a modification of technique had been employed, and believed that this procedure protected the blood supply to the parathyroids. Our observations lead us to suggest that he was thereby actually protecting the glandule itself rather than its blood supply.

In 1927 we were employing a standard type of thyroidectomy which included removal of the lateral capsule with the partial lobectomy. At this time Millzner, working in the laboratory of surgical pathology, after familiarizing himself with the gross characteristics of the parathyroid, found at least one glandule in twenty-eight per cent of our removed specimens. By marking the anterior capsule of each lobe before removing it, the exact location of any parathyroids on the specimens could be determined.

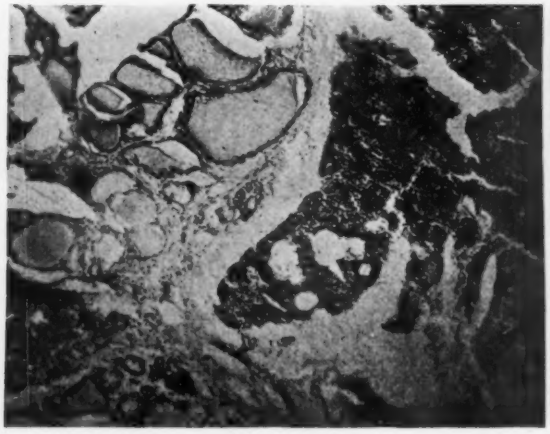

Fig. 2.

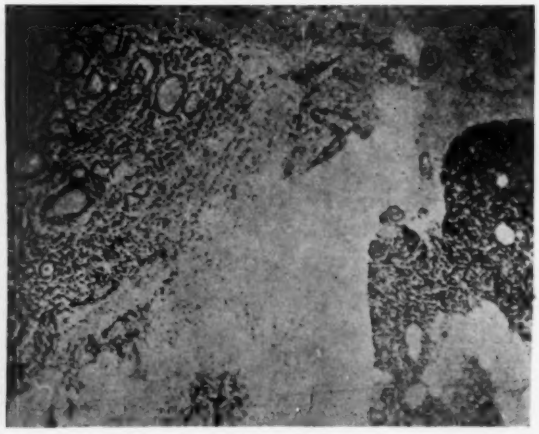

Fig. 3.

In a sketch representing the anterior and lateral capsule, as usually removed it was then possible to plot the location of all parathyroids found (Fig. 4).

This diagram serves clearly to show the danger zones of the lateral capsule at the inferior poles, the presence of parathyroids

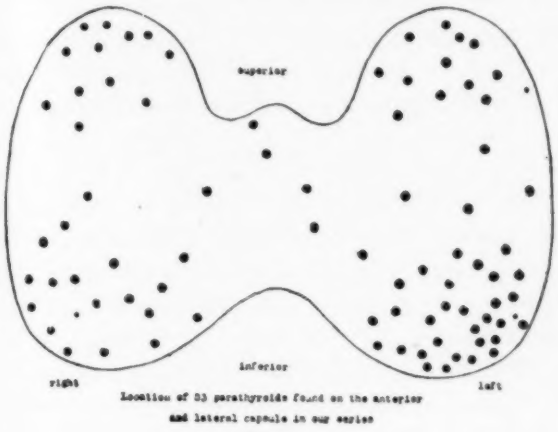

Fig. 4.

occasionally on the anterior capsule, and a fairly frequent location anteriorly at the superior poles.

Investigation was then transferred to the anatomical laboratory and the autopsy room where again in 30 per cent of cases one or more parathyroids were demonstrated on the lateral or anterior thyroid capsule.

That these observations are not limited to our own clinic was easily shown for we have found parathyroids in specimens in the laboratories of several of the large goiter clinics of this country, in one instance five in the first three specimens examined, in another, four in the first eleven.

The usual technique employed in partial or subtotal thyroidectomy involves removal of the lateral capsule. The findings outlined above would appear to warrant a modification of this procedure so as to include a careful search of the anterior and lateral capsule for parathyroid glandules, and then to preserve the lateral capsule and any parathyroids noted. This modification is particularly applicable in the operation of subtotal thyroidectomy for exophthalmic goiter or the large adenomatous goiter (Figs. 5 and 6).

As a further protective measure, as suggested by Lahey, the removed specimen may be carefully searched under aseptic precautions and any parathyroid tissue found may be reimplanted.

In our campaign for parathyroid preser-

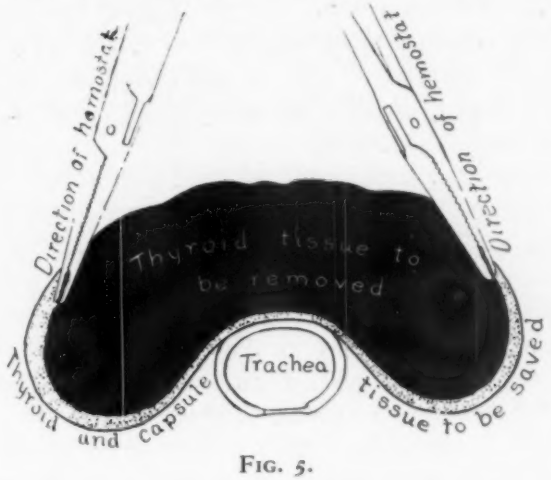

Fig. 5.

vation we have frequently met the argument that it makes little difference whether or not one or even two parathyroids are removed for no evidence of their deficiency has followed. If routine tests for the subtetanic stages are employed, I feel certain that such evidence will frequently be

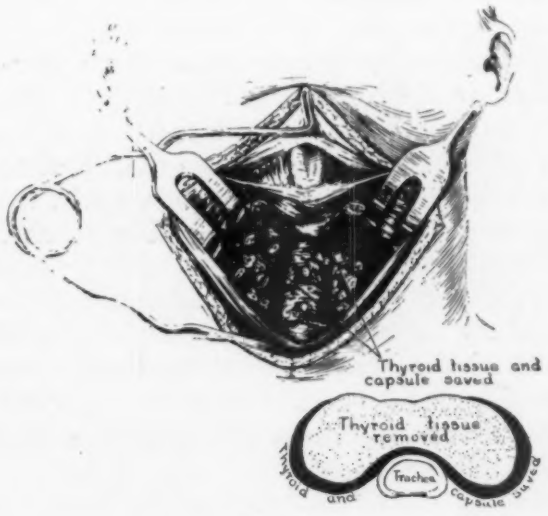

Fig. 6.

encountered, even though but one glandule be injured or removed.

In closing it would therefore appear safe to state, even with our present knowledge, that these tiny bodies have a tremendous influence on the human physiology and that, having this importance, every effort should be made to conserve them.

ETIOLOGY OF GRAVES' DISEASE*

E. P. Sloan, M.D.

BLOOMINGTON, ILL.

A Hypothesis. *The etiology of Graves' disease is hyperplasia or pathological changes in the thyroid gland that are the result of thyroiditis or infection involving the gland substance.*

Clinical, experimental and pathological evidence all point to the thyroid as the site of primary disturbance in Graves' disease. We must admit that there is much evidence that the sympathetic nervous system and many of the other ductless glands are involved but the combined evidence of clinical, experimental and pathological research indicates with a reasonable degree of certainty the correctness of the following premise: *In Graves's disease the thyroid is the bellwether of the endocrine insurgents and the other glands follow in the path of endocrine imbalance.* Thyroid dysfunction is the *cause;* general or other endocrine dysfunction is the *effect.*

Further proof of the correctness of that premise is afforded:

1. By the fact that ligation, injections into the gland, or removal of any appreciable amount of gland substance is followed by definite improvement.

2. The recurrence of symptoms after operation are always synchronous with increase in size of the remaining portion of the thyroid.

3. If the portion of gland removed is carefully examined, areas will be found in which the typical, characteristic changes called hyperplasia are evident. If we admit that the change in the structure of the substance of the gland known as hyperplasia is the actual etiological factor in the production of Graves' disease, then the problem of the etiology of Graves' disease is narrowed down to a consideration of the cause of the hyperplasia. The problem then becomes one of discovering the cause of hyperplasia in the thyroid.

No convincing evidence has been presented to show that hyperplasia can be produced in a normal thyroid by parathyroid deficiency, cardiovascular changes, pituitary, thymic, pancreatic or adrenal dysfunction or sympathetic excitation.

TOXIC THEORY

Some observers have presented credible evidence to show that poisoning by phosphorus and other chemicals, as well as by toxins of intestinal origin, *sometimes* results in thyroiditis and as a result of the thyroiditis, hyperplasia has occurred. Apparently conclusive evidence has been presented that thyroiditis is often followed by hyperplasia but the evidence presented that the thyroiditis is due to poisoning by chemicals or toxins of intestinal origin is in only few cases conclusive. If we accept this theory, and it has not been successfully controverted, its application is limited to the small percentage of such cases in which the possibility of such poisoning cannot be excluded with reasonable certainty.

GASTROINTESTINAL THEORY

Gastrointestinal infection is considered of great importance by McCarrison, Lane, Bainbridge and others, and is, undoubtedly, often indirectly an etiological factor, but none of them has presented conclusive evidence that this etiological factor is present except in rare cases.

INFECTION THEORY

Many investigators have tried to confirm the theory that the hyperplasia is due to infection by searching for the infective organisms in the specimens of gland removed.

In 1914 Rosenow isolated a non-hemolizing streptococcus from the thyroid gland in 25 of 32 cases of thyroid enlargement, most of which were of the exophthalmic type. Other investigators have produced much but not conclusive evidence. The search for the infecting organism in specimens removed at operation

* Read at the Annual Meeting of the American Association for the Study of Goiter, Dayton, March 25–27, 1929.

has, on the whole, been very disappointing. From the clinical standpoint, however, there is much evidence that is apparently conclusive. The evidence and support of this theory must necessarily be almost entirely clinical.

Vincent and others have noted the thyroid enlargement that is often present in acute articular rheumatism. Beebe found a history of repeated attacks of tonsilitis in 40 per cent of his hyperthyroid cases. Charles Mayo lays much stress on the relationship of hyperactivity of the thyroid gland and focal infection. Numerous other writers might be quoted who have by clinical observation and animal experimentation proved that infection is a most important factor in the etiology of Graves' disease.

But can we go farther and say that *the* etiological factor in Graves' disease is infection involving the gland itself?

Admitting that the infective organisms themselves can rarely be found in the portion of gland removed, and ignoring the evidence of previous infection afforded by pathological changes consistently found in specimens removed, can we produce credible evidence in support of our hypothesis that the etiology of Graves' disease is hyperplasia or pathological changes in the gland substance from thyroiditis or infection involving the gland itself?

It can rarely be demonstrated that any of the known infective organisms are present in the portion of gland removed at operation. Shall we accept this fact as evidence that infection has not been present? We do not expect to find the infective organism responsible for an orchitis in the specimen removed months or years afterward. We accept the pathological changes present as evidence of the previous infection.

We may say the same of ovarian, kidney, gall-bladder, lung and many other infections. Rarely do we find gonococci in the specimen removed at operation for chronic salpingitis.

PHYSIOLOGICAL CONSIDERATIONS

Secretion. It seems, in the present state of our knowledge, that we must believe either that the thyroid has the faculty of multiple secretion, or that the cell which, according to the holocrine theory, constitutes the secretion, contains multiple activating agencies. We cannot conceive, for instance, of iodine as the sole activating agency. There is a decided difference in the action of iodine and thyroxin on the normal individual. As well as the iodine in the colloid, there must be another secretory product to complement the iodine to produce perfect thyroxin. The "element x," as we may call it, may be pictured as constituting approximately 35 per cent of the thyroxin molecule. It may fuse with the iodized colloid in the follicle, or if no iodine is present in the follicle, it may enter the circulation as a toxic product. If sufficient iodine is present in the blood, it may combine with the iodine in the blood stream and form thyroxin.

Genesis of Colloid. There are in general two theories of colloid secretion, the merocrine and the holocrine. According to the merocrine theory of secretion, the secretory product is evacuated into the follicle by rupture of the nuclear membrane. The cell is not destroyed, regenerates and resumes its function. According to the holocrine theory the whole cell is used in the process of secretion and is destroyed. Most authorities favor the merocrine theory; some agree with Florentin, the French histologist who in exhaustive experiments on the guinea pig, found that holocrine secretion is responsible for the production of colloid. He finds that the whole cell, nucleus and cytoplasm, degenerates into colloid substance. We agree with some observers who believe that colloid results from both the holocrine and merocrine types of secretion.

The interstitial cells are located in the connective tissue between the follicles and their arrangement is very irregular. They are often arranged in cords of columns or piled-up epithelial masses. In infants these interstitial cells are very abundant

and greatly predominate over the acinal cells so that large areas of the thyroid are without follicles.

As regards the function of these cells, recent work seems to show that, as well as similarity in structure, they possess function similar or identical to the function of the acinal cells; that, in fact, they can take part in the formation of new acini. New follicles may form from a proliferation or budding-out of the eipithelial cells lining the original follicle.

Undoubtedly, acini may originate in this way; however, new acini are more commonly formed from the interstitial epithelial cells. The cells in the center of a little island of epithelial elements may undergo nuclear changes and cell division; proliferative and degenerative changes occur, the cells are completely broken down and a minute quantity of colloid appears which increases with increase in size of the follicle.

That the interstitial cells should remain absolutely inactive until such time as they have opportunity to engage in follicle formation seems very improbable. There is much evidence to show that secretion of colloid according to the merocrine theory does occur. There is also convincing evidence to show that the cell does finally disintegrate and the nucleus, cell membrane, and cytoplasm all find their way into the acini. That the final disintegration of the cell does not, to any great extent, enter into the secretion of colloid seems to be proved; so what is the function of this final disintegrated cell?

Our Hypothesis. Secretion of colloid occurs in the interstitial cells. By rupture of the cell membrane the colloid is released and finds its way into the acini.

The cell finally becomes one of the cells lining the acini, is exfoliated, disintegrates, releasing into the acini the unknown "element x" of thyroxin. The "Element x" contained in the nucleus and the cell membrane having a great affinity for iodine, combines with the iodine in the colloid, producing wholesome thyroxin, that finds its way into the general circulation by the way of both the capillaries and lymphatics. If iodine is not present in the colloid in the acini, thyroxin is not elaborated and the "element x" enters the circulation as a toxic substance.

When infection attacks the gland, the bountiful blood supply usually prevents abscess formation. But the inflammatory reaction or thyroiditis produces changes in the secreting cells that checks or destroys the secretion of colloid by rupture of the cell membrane, namely, by merocrine secretion. The cell membrane does not rupture and release colloid into the follicle. No excess of iodized colloid is present in the follicle when the cell containing some of the "element x" in its nucleus and cell membrane reaches the follicle and disintegrates. No iodine being present in the acini, the "element x" enters the circulation as a toxic product.

If the blood stream is iodized, the "element x," having a great affinity for iodine, combines with the iodine in the blood stream and wholesome thyroxin results.

Argument. From the clinical standpoint this hypothesis provides a satisfactory working basis. Over 30 per cent of the cases of Graves' disease that we see present a history and findings that most strongly supports this hypothesis.

We have not seen a case of Graves' disease in years in which a history could not be obtained of some focal or systemic infection that had occurred shortly before the advent of symptoms. In the cases of toxic adenoma with the type of toxemia seen in Graves' disease, the type called "secondary Basedow's" in Europe, almost all of them present a history of some infection, systemic or focal, shortly preceding the onset of symptoms of toxemia.

As long as the blood stream can be kept iodized the symptoms are controlled.

We have seen many cases of thyroiditis that we expected to be followed by Graves' disease and over 50 per cent of them have developed Graves' disease within a few months.

THYROID AND REPRODUCTIVE ACTIVITY IN THE FEMALE

A PRELIMINARY STUDY*

RALPH R. WILSON, M.D., F.A.C.S.

KANSAS CITY, MO.

WITH the development and intensification of "specialties" in medical practice, it is realized more and more that the female organism must be considered as a unit, combining together multiple and intricate systems, which work in peculiar accord. Of these intricate systems, naturally the one possessing the function of reproduction is of chief importance and among the factors exerting an influence upon it is the thyroid. This influence is yet imperfectly determined; nevertheless certain stepping stones are afforded in the study of their relationship. For purposes of expediency it is probably better to consider thyroid activity as emanating from the "thyroid system" instead of a single gland, because of the well recognized interplay of the thyroid, the pituitary and the ovary.

Considerable evidence is now at hand supporting the addition of the pancreas to this triad, e. g.: Vogt has recently reported the production of sterility in animals by the use of insulin injections only. Also, the occurrence of fatty stools in Graves' disease is so frequent that it is difficult to assume that it is purely casual. Perhaps the parathyroids have an unsuspected link in the chain too, for how otherwise can the infrequent occurrence of gastric tetany be explained in the severe cases of vomiting of pregnancy?

It is interesting to outline the normal behavior of the reproductive and thyroid systems before considering the abnormal manifestations.

NORMAL FUNCTIONS

The woman is strikingly feminine before the power of reproducing is acquired and remains so even after losing this power. That such an epoch can transpire with so few ill effects is due to the close relationship of the various body systems among which the thyroid is not the least.

In utero both primordial ova and primitive thyroid cells are laid down in the first weeks of life and begin to function soon thereafter, both working together more or less, in body development. In postnatal life, however, it is significant that these systems become antagonists, so to speak. The absence of the influence of the reproductive system contributes to a characteristic lengthening of the long bones while in the absence of thyroid activity these same bones are excessively shortened.

At the onset of puberty there is a coincident increase of activity of both, manifested on the one hand by sexual power and on the other by increased metabolism and even actual thyroid enlargement. Likewise during the sequence of menstrual cycles there are vasomotor disturbances possibly attributable to thyroid secretion instead of ovarian. It is a well known clinical observation that a large per cent of women show visible evidence of thyroid enlargement in the early menstrual stage. If menstruation is delayed a greater enlargement is perceptible. Lange is of the opinion that this enlargement is purely physiologic representing a cyclic hyperplasia rather than pure hyperemia, as once was held. Opinions are still at variance, however, as to whether or not these individuals are more likely to develop goiter in later life.

Ramos and Schteingart report that 61 per cent of women show, in pregnancy, an increased metabolism among the normal

* Submitted for publication January 26, 1929.

cases. Practically all cases of pernicious vomiting, however, show a lowered metabolism and the successful use of insulin in its treatment again calls attention to the close relationship between the thyroid and the pancreas. That the thyroid frequently enlarges during early pregnancy is a matter of common knowledge, and Lange contributes the interesting observation that toxic albuminuria does not develop in those cases, suggesting a detoxifying function to the thyroid. After parturition the glandular enlargement generally subsides and the basal metabolism returns to normal, although in some instances this does not occur until lactation ceases. In the event of interruption of the pregnancy before term there is a tendency not only to rapid subsidence of the enlargement, but to a degree of actual hypo-activity of the gland, usually with few objective symptoms. W. P. Graves records cases of thyroid enlargement in non-pregnant women which subsided after the practice of venery was checked. It is well known that excessive coitus delays menstruation without pregnancy supervening. There may be speculation then as to whether or not it is the action of the thyroid or the reproductive system in excessive intercourse that actually delays menstruation. It is interesting in this connection to be reminded that castration in the young adult practically always leads to some degree of hypothyroidism.

With respect to the menopause, there are so many changes occurring at that time that it is difficult to single out the activity of the thyroid system. O'Keefe assumes that during the menopause and the time thereafter the thyroid plays a minor rôle as compared to the childbearing period. It is only logical to conclude that the normal thyroid takes on diminished function with the advent of hypoactivity of the whole endocrine chain, and probably is not alone responsible for such changes as occur in the skin, fat layers and vasomotor system as formerly attributed to it. On the other hand many menopausal irregularities can be directly traced to pre-existing thyroid dysfunction. Supporting the opinion that the body organism is less responsive to thyroid activity after the menopause is the fact that the use of thyroid transplants is conspicious by its absence in the hands of the "rejuvenation enthusiasts." Conversely, numerous instances of thyroid activity being stimulated by ovarian transplants have been reported.

Finally, worthy of note is the repeated observation in normally and well balanced individuals that the required dosage of glandular products of either the thyroid or the reproductive system is considerably greater to produce perceptible effects than in those unbalanced cases with various dyscrasias.

ABNORMAL FUNCTIONS

A definite working rule cannot be established for classifying the reactions of the female reproductive system to thyroid diseases; nevertheless, it is remarkable how frequently the statistics indicate infantile genitalia, precocious puberty, scanty menstrual flow, decrease of menstrual periods per year, low fertility, menorrhagia, and early menopause, when thyroid disease exists. In general, however, two outstanding premises prevail: First, although a certain amount of thyroid secretion is essential for the well-being of the individual, excessive amounts have an influence upon the female reproductive system similar to other systemic poisonings as for instance, tuberculosis, diabetes or even drug poisoning. Its manifestation depends upon the particular decade of life at which it occurs but nevertheless is characterized by a retardation of normal function for that period. Second, and curiously enough, with lack of adequate thyroid activity there is also a retardation of normal function, as for example in cretinism and myxedematous states.

Answering these opinions offered to the contrary, it is only necessary to recall the frequency with which thyroid disease is associated with pelvic disease, the very

factor generally responsible for exceptions to the two above conclusions. In other words, in those instances of menorrhagia in Graves' disease or in myxedema there is often adequate cause to be found in the reproductive system alone. It is the experience of many that goiter is frequently associated with pelvic symptoms and in most instances these symptoms indicate definite pathology. Further support of such close relationship between the thyroid and female reproductive system is the ratio of thyroid disease in women as compared to its occurrence in men.

In the presentation of abnormal functions of the thyroid and reproductive systems it is more practical to classify thyroid disease and discuss in each group the effects on reproduction. In the classification that follows no claim is made to perfection, inasmuch as a gynecological clinic affords too few thyroid patients for their adequate study and grouping.

1. CONGENITAL THYROID DISEASE

a. Bram reports goiter at birth both with and without signs of hyperthyroidism. Schlesinger also reports goiter in the newborn but states that this occurrence is in endemic goiter areas or in goitrous parents. Practically all newborn with toxic symptoms show subsidence in a few weeks due to the transiency of the hyperplasia. Therefore any relationship to the reproductive system is remote, in these cases, although some consideration must be given the thyroid in those cases of precocious puberty usually credited to the pineal body and adrenal glands. In those children manifesting precocities the associated thyroid enlargement is more frequent than in adults and the actual enlargement is more perceptible.

b. Cases of adenoma at birth are recorded but occurring at this age of life one of two things usually occurs: either the death of the child, or more often surgical intervention relieves the condition before any influence is exerted upon reproduction. In no wise is this group to be confused with the histological group in adults designated as "fetal adenomata."

c. In cretinism menstruation either develops late, or not at all, presenting typical infantile internal and external genitalia. Experience in the untreated cases is so rare that there is little more than speculation concerning pregnancy therein. Under treatment, began early and persistently maintained, the improvement may be astounding yet nearly all come into puberty several years late. In many cases the cycle is apparently normal but as a rule infantilism, frigidity and low fertility are frequent. There may be long periods of amenorrhea. In the event of conception their pregnancies are characterized by a tendency to miscarry and, due to the generally contracted pelvis, usually are terminated by cesarean section. The menopause nearly always occurs several years early and is peculiarly free of severe constitutional reactions, probably because most of the patients are receiving thyroid medication at the time; this O'Keefe has found to be beneficial in many of the disorders associated with the menopause.

2. ADOLESCENT GOITER

This group, in which there is mere presence of goiter, shows no variation from the normal in menstruation, conception or delivery. J. Forest Smith however reports in 100 cases of adolescent goiter, 79 per cent of the colloid variety. He adds the further significant observation that the menstrual flow "is often diminished or absent when hyperthyroidism is present, and excessive when thyroid activity is below normal." A small percentage of adolescent goiters show hyperactivity. Of these some are the true thyrotoxic type. The others are the colloid type which have had early but transient increase in activity. In middle life or later years O'Keefe observes, "I have never seen a case of hypothyroidism with menorrhagia which was not complicated by definite pelvic pathology."

The colloid variety in this group ad-

vances into one of three stages. First it may be later associated with adenomatous growths and subsequently grow into the variety of toxic adenoma; second, it may develop malignant tendencies, particularly after the age of twenty-five or thirty; third, it remains as colloid goiter with varying degrees of hypoactivity throughout life. Guthrie is definitely of the opinion that these do not degenerate into myxedema in later years.

Those women afflicted with colloid goiters of the third type miss much in life. They are apathetic, they are victims of infection and they are often called hypochondriacal. Sexually they may be fertile but often indifferent. In pregnancy they tend to miscarry in the early months but evading this, they then more or less successfully give birth to oversized children. They may acquire large families, most probably due to apathetic acquiescence rather than actual desire. Their menopause is terrible unless rescued by thyroid therapy. The more marked the hypothyroidism the more marked and progressive are the above enumerated symptoms. A large number of these cases have no visible glandular change and therefore require detailed clinical and laboratory study for an accurate diagnosis.

3. ADENOMA

Adenomata without symptoms, in reference to the reproductive system, remains thus a relatively short length of time. They naturally progress into toxic states but menstruation, pregnancy, and menopause hasten this progression. In a given adenoma it is fairly safe to asxume that amenorrheic tendencies signify increasing toxicity, while menorrhagia and metrorrhagia indicate colloid deposition. As with most types of thyroid disease, adenoma progresses by remission and by so doing there may be alternating periods of amenorrhea and menorrhagia.

Multiple or substernal adenoma may be a serious complication in labor by causing suffocation purely by mechanical means.

Toxic adenoma in relation to the reproductive system is little different from true Graves' disease except in the management of pregnancy. It comes on in later years in an organism already damaged more or less by the wear and tear of life. Successful pregnancy requires a good reserve. Adenomata take on toxicity slowly as compared to exophthalmic goiter and more time is afforded for study of the case before outlining procedures. In a given case of toxic adenoma complicating pregnancy when the patient's condition requires relief, it is probably better to attack the thyroid first; while the converse procedure will probably give better results in true primary thyrotoxicosis.

4. ACUTE HYPERTHYROIDISM OR THYROTOXICOSIS

If the onset is before puberty, menstruation is delayed and underdevelopments of the generative tract are frequent. After puberty there are amenorrheic tendencies in the majority of the profoundly toxic. There is a smaller percentage, however, to whom the toxin is a tremendous stimulant. These usually have a fairly normal menstrual cycle which is peculiarly free from distress and they have great difficulty in maintaining sexual continence. The former type usually are sterile but if pregnancy supervenes it usually ends in a catastrophe. If they succeed in overcoming early nausea they are so weakened by lack of food that the disease itself overwhelms them. Pregnancy in the latter group often ends in abortion, considerably more frequent than in cases of hypothyroidism, due chiefly to extraneous factors as indiscretions with reference to exercise, coitus etc. During the latter part of pregnancy and the lactation period there is only occasionally an aggravation of the thyroid symptoms. First labors are particularly dangerous to the baby due to titanic contractions and premature births. Multiparous labors are short in these cases and the child withstands the ordeal better. With respect

to the mother two fundamentals are to be kept in mind: First, the heart must be guarded against sudden failure; and second, due to the known tendency to poor coagulation time, there may be alarming postpartum hemorrhage requiring uterine packing and hemostatic medication systemically. Both these groups are inclined to pass the menopause earlier than the average woman but go through it quickly and with comparative ease. Following this a natural remission of the disease may occur and the woman be normal again.

Williamson points out that if these cases have thyroidectomy, at least two years should elapse before attempting pregnancy again even though there be complete alleviation of symptoms before that time. If there are two or more living children already, it is probably wise to advise against any future pregnancies in view of the likelihood of relapses.

With reference to therapeutic abortion the gynecologist must be on guard for a marked improvement in the patient's condition following the emptying of the uterus and subsequent refusal of thyroid surgery until the predicament again occurs. In the primary type of thyrotoxicosis complicating pregnancy, or vice versa, it is probably a better procedure to empty the uterus before surgically attacking the thyroid because of the preexisting tendency to miscarry and the narrow margin of safety in postoperative recovery with the fetus in utero.

5. MYXEDEMA

Myxedema comes late in the reproductive life of a woman. H. Gardner Hill and J. Forest Smith report a series of cases in which menorrhagia was the outstanding symptom where the onset was before the menopause. They further report that those women developing myxedema after the menopause, had no particular distress in passing through the climateric even in cases where it was definitely premature.

As previously stated, the artificial menopause is followed by a degree of hypofunction of the thyroid and in rare instances leads to typical myxedema. It is only fair to assume, however, that in this event there must have been some pre-existing thyroid dysfunction which was augmented by the castration.

CONCLUSION

It is the object of this paper to point out the different relationships between the thyroid and the reproductive systems. In other types of thyroid disease, as malignancy, tuberculosis etc., there is as yet not sufficient data of characteristic nature to make it profitable to include them in a discussion of this type.

Finally, one cannot progress far into the study of either the reproductive system or the thyroid in the female without being impressed with their close relationship.

ANOMALIES OF THE URINARY TRACT*

N. P. RATHBUN, M.D., F.A.C.S.

BROOKLYN, N.Y.

THIS title indicates a subject which is obviously altogether too comprehensive in its scope to warrant any attempt to cover all phases of it in any one paper of reasonable length. I have elected therefore to stress what appear to me to be some of the more important clinical phases of the subject, based rather largely on my own personal experience, gathered from cases occurring in my clinic during the last five years. The bibliography on this subject is enormous and is of course reasonably familiar to all of us. The embryology is very interesting and extremely important for an intelligent conception of many of the anomalies noted. However, that by itself is a very large subject; volumes of readily available literature have been written upon it and it will be only casually referred to in this paper.

I believe that anomalies of one sort and another are noted more frequently in the urinary tract than in any of the other body systems. This may perhaps be explained in part at least by the extremely complicated embryological development. These various anomalies have been noted from time to time since time immemorial; usually, however, at first, as autopsy curiosities, a little later as accidental findings noted in the course of operations either upon the urinary tract or some of the abdominal organs. It is only in recent years, since the development of modern methods of diagnostic urology, that these conditions have been regularly recognized in the course of a routine examination and their relation to co-existing pathology evaluated and proposed measures of surgical relief properly interpreted. However, even with all of our modern methods, we are still considerably below a 100 per cent standard of efficiency and this, to my mind, emphasizes the importance of a routine examination of the entire urinary tract, including urography in *all* cases where there is a suspicion of any pathology above the bladder. By following this practice, while we will no doubt continue making some mistakes, I am sure we will materially reduce our incidence of error and incomplete diagnosis.

It would seem fair to say that the only possible valid objection to such a policy is the possible risk involved. For several years past we have made an average of several hundred pyelograms annually and since using the 15 per cent solution of sodium iodide, I have seen only one case in which there was any reaction sufficient to cause the slightest degree of worry. This was a recent case of ureter calculus, in which the necessary operation was hastened a bit. However, in this case the stone was removed, prolonged drainage instituted and the patient went on to complete recovery with a good kidney. I realize that this may sound like an extravagant statement and that my experience is somewhat at variance with that of other observers. However, it is given for what it is worth. If my experience is of any value it would seem to indicate that urography is a perfectly safe procedure and there can be no doubt of its value even in cases where it would appear that a reasonably satisfactory diagnosis can be made without it. Certainly many valuable points are added which might otherwise be easily missed. If we are going to do it eventually, why not now as a part of our first routine examination.

Many, I might say most of the anomalies of the upper urinary tract are by no means inconsistent with perfect health and have no clinical significance except in so far as they have a bearing upon associated pathology. There are, of course, exceptions to this, such, for example, as those cases in which a ureter, supernumerary or other-

* From the Urological Service, Brooklyn Hospital.
Read before the Section of Genito-Urinary Surgery, N. Y. Academy of Medicine, Dec. 19, 1928.

wise, empties outside of the bladder, as for example in the urethra or the vagina. Such cases, of course, present very definite pathological states and are suitable candidates for surgical relief. We will speak of this further a little later.

Some of the anomalies will be entirely omitted in this paper or merely mentioned in passing as, for example, the entire absence of both kidneys. A few such cases have been reported in non-viable fetus and have absolutely no clinical interest.

ANOMALIES OF THE VASCULAR SUPPLY

These occur so commonly in my experience that I have come to the point of rather expecting to find them in the course of operations upon the kidney. In fact I have often wondered if they did not have some bearing in the lesion present. It does seem to me that they are noted more commonly, in proportion, in the operating room than at the autopsy table. This, of course, may be because we look for them more carefully. The practical point is that they should be borne in mind in all our renal surgery and in performing a nephrectomy all firm bands, wherever located, should be clamped and ligated before dividing. In conservative renal surgery, they should with equal care be preserved.

The question of the relation of anomalous vessels to certain cases of hydronephrosis is one which has aroused a great deal of discussion and about which there is a considerable difference of opinion. Personally I doubt very much if an anomalous vessel is ever the sole course of hydronephrosis. On the other hand, I am perfectly satisfied that they are not infrequently a contributing factor and perhaps the one factor which precludes the possibility of relief by conservative measures. I have in mind those patients who have had repeated attacks of pyelitis and whose general health has been undermined with a resulting loss of weight and muscle tone and a sagging of the kidney. I have seen a number of such cases, one very recently, in which the kidney was so badly damaged as to require nephrectomy. In this particular case there was a vessel about one-half the size of the renal artery entering the lower pole. The kidney and pelvis hung over this with a sharp angulation at the ureteral pelvic junction. The patient was a woman of fifty-two who had been in perfect health until two years before, when she had a sharp attack of pyelitis, complicating a gastrointestinal upset. It is often a difficult matter to know what is best to do in cases where we are undertaking to relieve symptoms and at the same time conserve the kidney. I have in a few such cases deliberately divided the vessel with apparently no appreciable damage to the kidney and with complete relief of symptoms, notwithstanding the fact that subsequent pyelographic studies have shown no change in the picture. In other cases where it is obvious from the size of the vessel that its division would seriously interfere with the blood supply, we have a choice of kidney suspension in an effort to straighten out the kink or division and reimplantation of the ureter. I have had no experience with the latter operation.

Just a word about the so-called floating kidney. They were quite fashionable twenty years ago and were often subjected to unnecessary and meddlesome surgery. Fortunately we have passed that stage in our development and I think we all recognize that the prolapsed kidney occasionally noted in the course of a routine abdominal examination or which exists as a part of a general ptosis of all of the abdominal viscera is better without surgery. On the other hand I occasionally see a patient who has a kidney with an abnormally long pedicle, which permits of a very wide excision and who has very definite symptoms from it such as a more or less constant ache or repeated colics or both. If these patients are not relieved by a suitable belt, and it has been my experience that they usually are not, I believe they are suitable candidates for a nephropexy. I have done this operation a number of times with entirely satisfactory results.

THE APLASTIC KIDNEY

This item is of particular importance in reference to the ability of such a kidney to sustain life in the event of disease or removal of its fellow. It has been pointed out by some observers that in such kidneys the dye tests will show a normal time of appearance after either intramuscular or intravenous injection but that the percentage of output over a measured period of time will be subnormal. This is of obvious importance when surgery is contemplated on the other side. While it is somewhat apart from the subject, I must confess to being somewhat heterodox on this matter. In my opinion the time of first appearance of either the red or the blue dye in a differential function test is quite as valuable as the percentage test as ordinarily performed. It is at least positive and the percentage test is not unless care is taken by plugging the ureter sufficiently to prevent flux around the catheter. I have only seen 3 of these aplastic kidneys. One was in a patient whose other kidney was the seat of tuberculosis. Because of rather extensive tuberculous lesions in other parts of the body he was not considered operable. Fortunately for me perhaps in each of the other two instances the symptoms were directed to the aplastic kidney. In one case a kidney rather less than one-quarter the size of a normal kidney but apparently normal in every other way was removed because of pain which seemed sufficiently great to warrant such a procedure. The operation was followed by entire relief from pain. It is of interest to note that in this case the time of first appearance of the dye test was markedly delayed and in about the expected proportion to the diminution of the percentage output. The other case also presented the symptom of pain but it did not seem enough to warrant any radical surgical measures.

FIG. 1. Unilateral fused kidney.

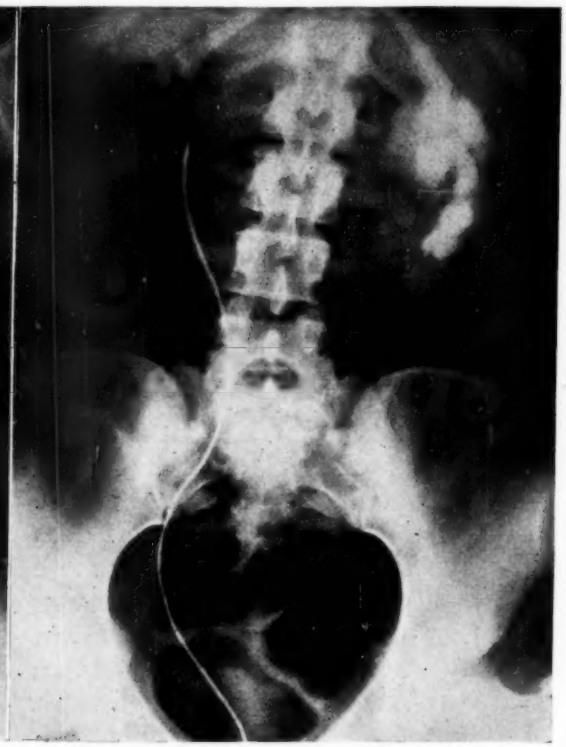

FIG. 2. Pyonephrosis of one-half of horseshoe kidney.

POLYCYSTIC KIDNEY

While there are a number of theories as to the nature of this condition, it is

rather generally conceded that they are congenital in origin, the most commonly accepted theory being that of Hildebrand

Fig. 3. Hydronephrosis, horseshoe kidney.

Fig. 4. Horseshoe kidney, normal otherwise.

that they are due to a failure of union of the collecting tubules with the metanephrogenic anlage. It is of interest, however, that the clinician rarely sees these cases until adult life. In fact most of my cases have been noted in patients in the fourth or fifth decade and they have usually sought advice because of an appreciable adbominal tumor associated with varying degrees of discomfort. A few have noted gross hematuria as their first symptom. This group may sometimes be difficult to differentiate for renal neoplasms. The pyelogram is rather characteristic but might in some cases be easily confused with the pyelogram of a renal tumor. Polycystic kidneys, however are practcially always bilateral so that bilateral pyelograms (made at separate sittings) plus the definite evidence of renal deficiency as shown in the blood chemistry and dye tests, should in the majority of cases clinch the diagnosis.

I have had one case in a woman of fifty who presented the symptoms of hemorrhage, pain and a palpable tumor in whom, while we made a provisional diagnosis of polycystic kidney, we felt that we could not exclude neoplasm and she was explored. At operation we found a large polycystic kidney. A large number of cysts were incised and collapsed and this procedure was followed by a marked improvement in all the symptoms, including the renal function and a striking change in the pyelogram. This operation was done three years ago and the patient remains in good health with no recurrence of the bleeding, which had recurred frequently during the two years preceding the operation. It is rather difficult to understand the why and the wherefor of all this but the same result has been rather frequently noted by other observers.

I have had one other very similar case in a man of fifty. In this case also the operation was undertaken because we were not certain of our diagnosis. The same procedure was carried out and

the same happy result followed. These are the only cases of polycystic kidneys upon which I have operated and those to be among the very rare forms of renal anomalies.

I have seen but 1 case of unilateral

Fig. 5. Polycystic kidney.

Fig. 6. Low kidney.

experiences might tempt me to adopt such a general policy.

Nevertheless I believe that most of the cases are better without surgery and should be placed in the hands of a competent internist.

We have had 2 cases of solitary cyst, both diagnosed as tumor because of bleeding and the pyelogram and both were successfully resected.

Most of these cases which I have seen reported have been subjected to nephrectomy. I believe this in many cases is entirely too radical. It would appear to me that these are ideal cases for conservative surgery, particularly where they are noted at one or the other pole, as was noted in both of my cases.

SUPERNUMERARY AND UNILATERAL KIDNEY

I have had no personal experience with supernumerary kidney and I believe this kidney. This occurred in the private practice of my associate Dr. W. F. McKenna. This patient had also a uterus didelphys. The case seems to have been proven with reasonable certainty by the fact that repeated cystoscopies disclosed only one ureter orifice in the bladder and by the fact that the gynecologist who performed an exploratory laparotomy could not palpate a kidney on that side. Entire absence of one kidney is, of course, to be distinguished from unilateral fused kidney. Of this latter group we have had 4 cases, one of them complicated by calculus. The ureter orifices are usually found in their normal situation, the ureter on one side crossing over above the bladder. In 1 of my cases the ureter in the side where the kidney was absent bifurcated at the sacral promontory before crossing. This patient complained of pains in the groin and while we recognized the

anomaly, we also made an incorrect diagnosis of stone in spite of negative roentgenograms. We based our diagnosis on the obstruction noted with the catheter at the point of bifurcation, plus what we interpreted as scratch marks on a wax tipped bulb. At operation no stone was found and we were able to demonstrate the course of the ureters and the entire absence of a kidney on one side.

Fig. 7. Bifid ureter.

Fig. 8. Reduplication of ureter, unilateral.

The patient who really had a stone declined operation. His outstanding symptom was hematuria. The other 2 cases had no demonstrable associated pathology.

This condition is readily recognized by suitable urographic methods. If the pyelogram is first made upon the side where the kidney is located, our suspicions will be aroused by the fact that the pelvis is out of its proper relation to the rest of the kidney shadow and a later pyelogram made from the opposite side will complete the diagnosis. If the first pyelogram is made on this side the diagnosis is made at once. Whether we are dealing with entire absence of one kidney or unilateral fused kidney, the practical point is that these patients have only one kidney. It is almost inconceivable that such a kidney should be surgically removed in these modern days, yet such tragedies have been reported in the past and it is possible that they may occur again.

While this condition is of course rare, it has been noted with sufficient frequency to make it imperative upon the operator, no matter how great the emergency, such, for example, as trauma, to satisfy himself that there is another kidney, if necessary, by means of opening the peritoneal cavity and palpating. In operating upon these kidneys one must keep in mind the extreme variations in their source of blood supply. This requires but a mention.

HORSESHOE KIDNEY

The subject of horseshoe kidney, including a review of the literature, was discussed by the writer in a paper published two years ago and will be passed over rather

hurriedly here. Most of the cases reported were not accurately diagnosed prior to operation. I believe by the employment of routine urography most of them will be diagnosed in the future. The characteristic roentgen-ray and urographic findings are of course familiar to every one.

Fig. 9. Reduplication of ureters, bilateral.

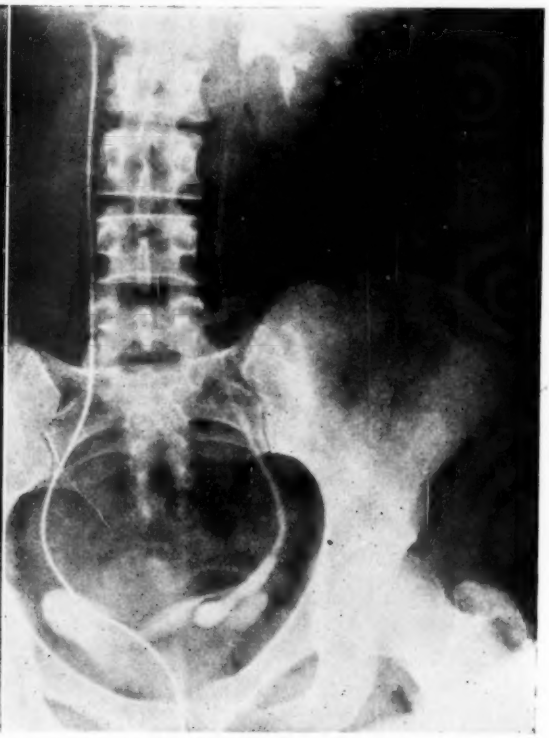

Fig. 10. Ureterocele.

Quoting briefly from my previous paper they may be summarized as follows:

The objective signs are most important and are largely those developed by the X-ray, particularly in conjunction with urography. A kidney shadow rather lower than normal and very close to the vertebral column is suggestive. In a good radiograph when the kidney outline is very clearly shown throughout except at the lower pole where the outline is very indefinite, it is strongly suggestive. In normal cases the inner border of the kidney forms an acute angle with the vertebral column at the upper end. The reverse is apt to be true in horseshoe kidney where the acute angle appears at the lower end. Shortening of one or both ureters as evidenced by the length of catheter passed is suggestive, and the reason for such shortening should be determined with horseshoe kidney as a possibility in mind.

Pyelography is undoubtedly the most important single procedure in making a diagnosis. In clinics where double pyelograms are made at a single sitting as a routine procedure, it would seem unlikely that the diagnosis would ever be missed. This is perhaps one argument in favor of such a technique. I believe, however, it is generally considered unwise so that we should learn to base our inferences on a single pyelogram made on the side under consideration. Our suspicions should be aroused whenever the kidney pelvis is found to occupy an unusual position, particularly if low or near the midline mesial to the ureters. This applies also to bizarre shapes, absence of calyces, or calyces overlapping the pelvis, or possibly directed toward the vertebral column. Such findings when noted should demand first, a very careful study of the radiograph for the purpose of outlining each pole of the kidney, particularly the lower; and second, a pyelogram of the opposite side, which should be carefully studied in conjunction with the original picture.

Most of these cases do not *per se* constitute a pathological state and it is usually only in the presence of associated lesions that they become of surgical interest.

We have had 8 such cases, 2 complicated by pyonephrosis of one-half of the kidney successfully resected through a loin incision.

One of these cases presented himself at the outdoor department with the symptom (and the only symptom) of urethral discharge, due no doubt to the irritating character of the pyuria. The cloudy second glass suggested the possibility of pathology in the upper urinary tract, and a routine examination, including pyelograms, made the diagnosis.

The other patient had pain plus pyuria noted by the family physician as a part of a general examination. Another case had a calculus removed through an anterior pyelotomy. This patient made a good recovery except for a sinus which persisted for about six months, owing to the irregular and tortuous course of the ureter. In some of these cases the pelvic drainage is not good so that delayed healing might be expected. In view of this fact it might seem wise in the absence of gross infection to make a special effort to carefully close the pyelotomy wound.

One other case was a woman who suffered from severe attacks of pelvic ache and pain which we attributed to one-half of a horseshoe kidney placed rather deep in the pelvis. We resected this by the transperitoneal route. The operation was followed by a rather gross wound infection, protrusion of the bowel, replacement under general anaesthesia, pneumonia and death. I believe because of the problem of drainage that wherever it is technically possible these cases should be approached through the retroperitoneal route.

One other case was discovered by one of our general surgeons in the course of an abdominal operation and was later turned over to us for pyelograms as a matter of personal interest.

The other cases were picked up accidentally in the course of a routine examination and had no associated pathology.

OTHER TYPES OF FUSED KIDNEY

There are a number of other types of fused kidney described at length in the literature, such for example as the so-called cake kidney, the solitary fused pelvic kidney, etc. I have had no personal experience with any of them. In the presence of complicating pathology they may present technical operative problems of great difficulty.

We have had two pelvic kidneys in each instance accompanied by a normally placed kidney on the opposite side. One was subjected to pyelotomy for calculus by the retroperitoneal route and the other to nephrectomy for pyonephrosis, also by the retroperitoneal route. In neither case was there any particularly great technical difficulty and both patients made good recoveries. The nephrectomy patient had two distinct sets of vessels, one coming from the aorta and vena cava and entering the upper pole, the other arising from the iliacs and entering the lower pole.

ANOMALIES OF THE URETERS

These occur so commonly as to be almost a weekly, certainly a monthly occurrence in practically every clinic of any size. They occur in great variety, such for example as complete reduplication on one or both sides, unilateral or bilateral bifurcation, practically always with the Y directed upward, bifid pelvis, trifid pelvis, etc. Supernumerary ureters occur sufficiently often to make it incumbent upon the cystoscopist, having located two ureters in their normal site, to make at least a casual survey of the bladder for the purpose of determining the possible presence of others.

In the great majority of cases the ureter anomalies are noted simply as curiosities and more often than not have no clinical significance.

One very practical point, however, is perhaps best illustrated by brief allusion to a case occurring in my practice several years ago, before the day of routine pyelograms and ureterograms. This was a patient who had an obviously tuberculous bladder with characteristic lesions about

one ureter orifice. Yet repeated examinations showed crystal clear urine from this side. Finally at one examination purulent urine with numerous tubercle bacilli was obtained. This apparent mystery was very simply solved at operation by noting the presence of a bifid ureter and double pelvis. At all but one of our catheterizations we had just happened to tap the healthy pelvis. The remaining half of the kidney was the seat of a caseous tuberculosis. A similar case was reported by Israel many years ago.

This also emphasizes one other point in the technique of making ureterograms and that is the advantage of making one ureterogram by injecting as the catheter is gradually withdrawn, entirely out of the ureter and out of the body. A bifid ureter might easily be missed by making the injection while the tip of the catheter is in or near the kidney pelvis.

It is only fair to say, however, that we have in a few of our cases secured a perfectly good picture of both ureters and both pelves with the injection made in this way. In a number of others the injection made from the pyelogram has shown only one pelvis while the injection made from the pyelo-ureterogram has shown them both.

There have been a few cases reported where the ureter has opened outside the bladder. I have never seen a case. Such a state of affairs should be considered among other possibilities in patients, particularly females who complain of a constant dribbling of urine plus the voiding of apparently normal amounts at normal intervals. These patients are suitable candidates for some form of surgical relief. In the absence of infection it would seem that simple ligation of the offending ureter should offer reasonable assurance of a cure. In the presence of infection it would seem more logical to resect the pelvis and corresponding portion of kidney as has been reported by Furniss and others. I should consider one of those two methods of attack preferable to reimplantation.

URETEROCELE

It seems fair to assume that this condition is brought about as a result of a congenital narrowing of the ureter orifice with a resulting obstruction and protrusion or herniation of the ureter into the bladder. It may be unilateral or bilateral. One of the prime points of clinical significance in this condition is the interference with adequate renal drainage with its consequent hydronephrosis, injection, etc. The diagnosis is readily made by their cystoscopic appearance supplemented by suitable roentgen-ray studies.

My associate, Dr. W. F. McKenna, in an article published about one year ago[1] collected 7 of these cases from our clinic.

They were all accompanied by varying degrees of hydroureter and hydronephrosis. Five of them apparently secured complete relief by simple dilatation, one was cured by fulguration of the ureter orifice. In the remaining case a plastic operation was done through a suprapubic cystotomy. The kidney in this case was, however, so badly damaged as to require nephrectomy a little later.

CONCLUSION

In conclusion, I realize that I have treated this rather large and very important subject in rather a cursory manner. It was, however, altogether too large an order to warrant any attempt to cover in all its phases so that I have as I said at the outset attempted in rather a rambling fashion to stress a few of the points which seemed to me to possess the greatest degree of clinical interest.

[1] McKenna, W. F. Ureterocele. *S. Clin. North America*, 7: 1001–1009, 1927.

HEREDITARY CONGENITAL ANOMALIES OF THE GENITOURINARY ORGANS*

HALSEY J. BAGG, PH.D.

NEW YORK

I SHALL report to you in this paper the results of experimental studies on certain congenital hereditary abnormalities of the genitourinary organs that were found in a strain of laboratory animals. This is a summary of the data collected during the last six years. It is based on the careful autopsy records of 5600 individuals. This group includes 1057 animals showing kidney defects respectively, of which 1000 have one or both kidneys missing at birth, and 48 in which one or both kidneys were found to be hydronephrotic soon after parturition. This summary also considers 17 animals in which one or both testes were abnormal.

After describing the stock from which these animals arose and the character of the hereditary behavior of the anatomical defects, I shall briefly summarize the statistical material and mainly confine my remarks to certain embryological studies that may throw some light on the much mooted question of the etiology of congenital solitary kidney, the bilateral anephridic condition, the solitary and bilateral hydronephrotic state, and finally the causation of the solitary testis.

About ten years ago the writer began a study of the effects of roentgen-ray and radium irradiation upon living organisms, and noted in this work the peculiar susceptibility of fast-growing embryonic tissues and the gonads to these physical agents. It was with the view of testing the possibility of altering the germ plasm of rats by means of radium irradiation that I first took up this subject in cooperation with Dr. J. F. Gudernatsch. The results of this investigation led to a more elaborate study in cooperation with Dr. C. C. Little in which we used the mouse as a subject. Time does not permit my entering into the details of this work and those interested in the subject are referred to the references appended to this article. It is sufficient to state that well-marked anatomical abnormalities have appeared in the descendants of roentgen-rayed male and female mice, the defects breed true, are recessive in character and behave mainly as mendelian in inheritance.[1] Such hereditary defects have not been found in a large number of control animals.

I have considered elsewhere the clinical significance of these studies. They bring to the notice of the medical profession a word of caution concerning the irradiation of women over the region of the ovaries when such women are in the child-bearing period. This caution also applies to the irradiation of the gonads in men when the product of these organs may enter into a pregnancy at some later date.

Only the parent generation animals, both males and females were roentgen-rayed. Certain of their unirradiated descendants in the third and subsequent generations showed the presence of congenital eye defects. This was the first type of abnormality to be found and it has bred true for 19 generations, extending over a period of six years.

In still later generations peculiar forms of limb defects made their appearance, clubbing, syndactylism, hypodactylism and polydactylism being the most prominent types. By selective breeding these abnormalities have also been intensified

[1] The experimental setting was as follows: Target-skin distance 12 in.; 2½ in. spark gap; 10 ma. of current and no filter. The animals were treated over the entire dorsal surface for twelve second exposures on each of five successive days. Twenty males and ten females were irradiated and were mated shortly after treatment.

* Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, November 21, 1928.

so that in certain litters as many as 7 out of 8 young have shown one or more defective limbs.

Embryological studies have shown that both the eye and the limb defects are very prominently associated with the formation of localized disturbances in circulation; in the former case in the periocular region and in the latter usually on the dorsum of the foot. There is apparently a temporary stage of lymphatic stasis which is soon followed by either a moderate or a relatively extensive extravasation of blood into the distended lymph areas in the subcutaneous tissues, with the resultant formation of a well-defined hematoma. The relative extent of this hemorrhagic process, its location in either the eye or the foot regions, and the period in which it makes its onset during the prenatal life of the animal, determine the type and degree of morphological change that will occur in later life. These observations are mentioned at this point because some such arrest in development associated with a blood vascular disturbance is probably associated with defects in the formation of the kidneys. The deep-seated location of the renal bodies however makes the observation of disturbances in this region exceedingly difficult, and it is only by considering certain well-recognized associated conditions such as hydronephrosis that we may obtain leads toward a tenable theory to account for the kidney abnormalities that this paper is largely concerned with. We shall return to a consideration of this matter after presenting the following data on the statistical study of the subject, so that you may know both the type and relative frequency of anatomical position of the kidney defects that have been referred to.

The first type of kidney defect was noted when some fifth generation animals were autopsied. They were descendants of the roentgen-rayed group. It was then found that certain of the animals had a so-called solitary kidney defect. A technique was perfected which enabled me to determine this condition in living animals. It consisted in lightly etherizing the animals and palpating for the kidneys. It was also found that the presence or absence of the left kidney could be detected in day-old animals by sight alone. At that time the skin is transparent in the newly born animals, the stomach is usually distended with milk and on this whitish background the spleen is readily distinguishable as an elongated dark red body. If a left kidney be present its inferior median border will show as a reddish brown body in the angle between the spleen and the mid-dorsal area of the body. When the left kidney is absent the stomach appears to occupy the left renal area. The right kidney may be felt after considerable practice in adult animals, but in day-old subjects it is so surrounded by the right lobes of the liver that it is not distinguishable by sight. If at least one kidney is present in the body there is a considerable amount of residual urine in the bladder soon after birth. The distended bladder can be readily seen through the body wall and carefully applied external pressure will cause the extrusion of urine. When both kidneys are absent at birth the left kidney is not visible, the bladder is collapsed and not recognizable by external view, and no urine will be extruded on pressure over the pelvis. Such anephridic animals appear normal in size, development and general body activity and ability to nurse, but show the usual signs of body edema, accumulation of abdominal fluid etc., about twenty-four hours after birth when they become comatose and die.

By breeding males and females with the solitary kidney condition the relative frequency of incidence of this abnormality was raised from 16⅔ per cent in unselected animals to 57 per cent in litters where both parents had the solitary kidney condition respectively. The following data have been obtained over a period of about five years during which especial attention has been paid to selective breeding for renal defects.

STATISTICAL SUMMARY

Results from 5600 autopsies.

Animals with kidney defects 1057.

Animals with one or both kidneys missing 1000; males 519, females 481.

Animals with one kidney missing 630; males 325, females 305; on right side of body 307, on left 323.

Animals with both kidneys missing 334; males 171, females 163.

Animals with a solitary kidney which was reduced in size, 25.

Animals with one or both kidneys hydronephrotic 48; males 27, females 21; on right side of body 29, on left 18; both hydronephrotic 1.

Animals with one kidney hydronephrotic and the other normal, 35.

Animals with one kidney hydronephrotic and the other missing, 11.

Animals with one or both kidneys reduced in size, 62 (reduction well beyond the limits of normal variability); males 36, females 26; on right side of body 31, on left 30; on both sides 1.

A study of this summary shows that in a strain of animals where there is a genetic tendency to disturbance in kidney development during prenatal life, and wherein selective breeding is instituted in order to intensify this defectiveness, an individual from this strain is nearly twice as likely to have the solitary kidney condition as it is to show the absence of both kidneys at birth; 630 to 334.

It is interesting to note that there is a slightly larger number of males than females in each of these groups, but the difference is apparently not significant; 519 males to 481 females. In like manner the left kidney is missing slightly more frequently than the right; 323 left to 307 right. Considering the 48 animals with one or both kidneys hydronephrotic, it is seen that the right kidney was the subject of this condition in 29 instances to 18 for the left kidney, and that only one animal was found with hydronephrosis on both sides of the body. There were 27 males to 21 females in this group.

When one comes to consider the possible explanation for these peculiar congenital anatomical abnormalities it will be well to note three other groups shown in the summary. One, the group of 25 animals with a solitary kidney respectively in which the remaining kidney was significantly reduced in size. This raises the question as to whether the pathological process or processes that resulted in the complete obliteration of one kidney might not also have been the cause of the appreciable reduction in size of the remaining kidney. In so far as these observations were made from autopsies performed soon after parturition, compensatory functional hypertrophy had not had sufficient time to increase the size of the solitary kidneys.

The second group in the summary that it is well to call especial attention to is that of 11 animals each showing a solitary hydronephrotic kidney respectively. Again in these instances I think it is legitimate to question as to whether the embryological disturbances that resulted in the hydronephrotic condition of one kidney might not have also been associated with the complete destruction or suppression of kidney development on the opposite side of the body.

And finally the third group of animals that is of interest is the one composed of 62 animals in which one or both kidneys were appreciably reduced in size respectively. This group may represent animals standing midway between the normal condition and those with markedly abnormal kidneys as described in the two preceding groups.

Before considering the questions raised in the above paragraphs there is still one more feature of the results that must be recorded as it bears a possible relation to the subject we are considering. In the same stock of animals in which the kidney defective group was found there were 15 individuals in which one or both testes were involved in a pronounced hemorrhagic process. Histological sections of these organs showed that the hemorrhage was

confined to the testis proper. It varies in extent from a diffuse extravasation of blood between fairly normal spermatic

missing right kidney as well and was blind in both eyes. One animal with a hemorrhagic left testis had a hydronephrotic

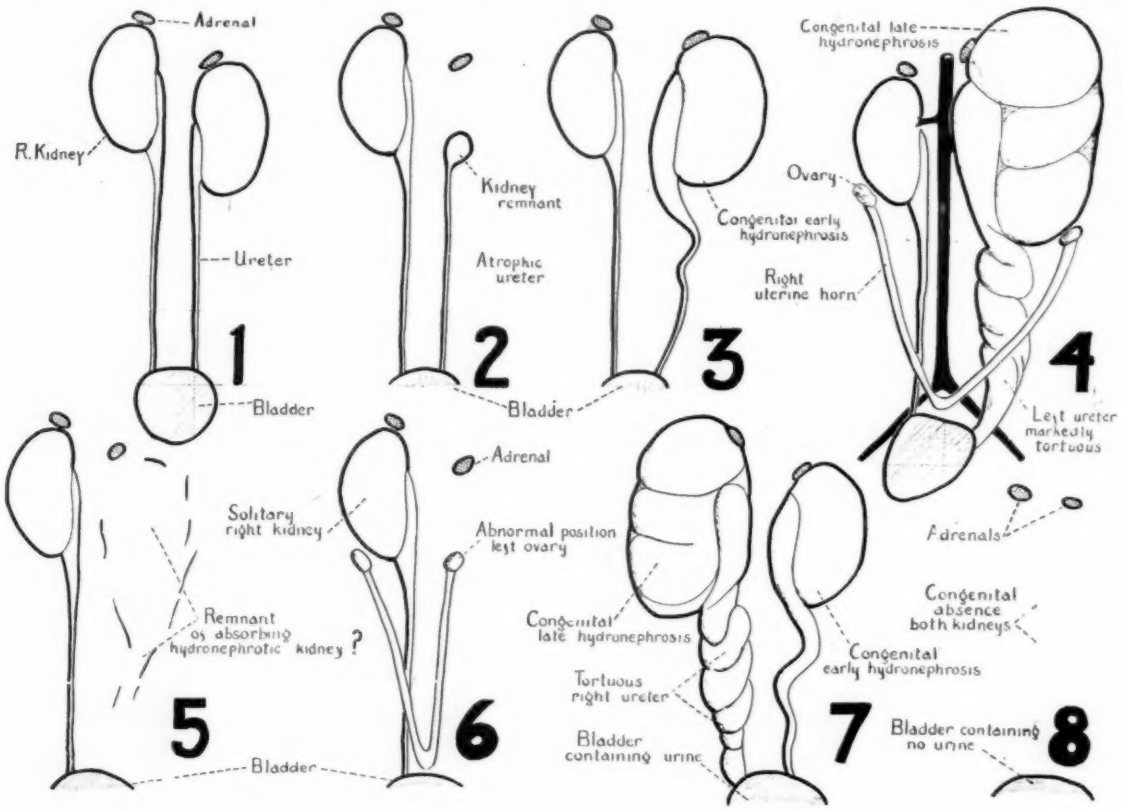

PLATE I.

FIG. 1. Diagrammatic sketch of normal kidneys, ureters, adrenal glands and bladder.
FIG. 2. Kidneys unequal in size, one at right being reduced to mere vestige.
FIG. 3. One kidney showing congenital early hydronephrosis.
FIG. 4. Congenital late hydronephrosis with tortuous ureter.
FIG. 5. Congenital absence of one kidney showing possible remnants of an absorbing hydronephrotic kidney.
FIG. 6. Solitary kidney condition. Note more medial position of left ovary and persistence of both adrenal glands.
FIG. 7. Bilateral hydronephrosis, both early and advanced types. Note presence of residual urine in bladder as recorded at parturition.
FIG. 8. Anephridic condition, showing presence of both adrenal glands and empty bladder.

tubules to a pronounced hematoma in which there remained but a few scanty remnants of degenerated testicular tissues. In 8 instances the left testis, in 5 the right, and in 2 instances both testes were involved respectively. In one instance an animal had a hemorrhagic testis that was observed through the body wall soon after birth, and in later life it was found to have that testis completely missing. In addition to the 15 recorded above 2 animals were found at birth each with a missing left testis respectively and one of these had a right kidney and was blind in the right eye. Another with a hemorrhagic right testis had a hydronephrotic right kidney, was blind in the left eye and its left front foot was clubbed.

Figures 1 to 12 inclusive illustrate the types of anatomical abnormalities that have been mentioned in the preceding text. I would call attention to the pronounced association of defects of the eyes and limbs that are associated with defects of the kidneys as indicated in the family charts.

DISCUSSION OF RESULTS

The strain of laboratory animals on which the study of this paper is based offers a unique opportunity for the careful observation of congenital abnormalities of the genitourinary tract as they occur spontaneously and not as a result of operative interferences etc. As far as I am aware this is the first and only strain of animals that has been reported as showing such congenital defects, and as the embryological plan of development in this mammal is similar to that for man it is perhaps justifiable for one to discuss the results that this laboratory strain has given in the light of the known congenital abnormalities of similar nature that have been found in man.

The embryological studies that have been undertaken in my laboratory indicate that the suppression of one kidney may occur either fairly early or relatively late in prenatal life. The results that I am now reporting are mainly confined to the conditions found very near parturition, but I shall briefly mention certain results that were obtained by Miss A. L. Brown, who while working in my laboratory was given for study earlier stages of embryonic development as seen in embryos from the strain of kidney defective animals. Certain data of her investigation have been published.[2] The point of interest in her results is that the suppression of one or both kidneys may occur at a relatively early embryonic stage and this suppression is correlated with the failure of one or both ureters to make contact with the developing blastema of the kidney. The ureter buds in respective animals were found to have stopped their growth at various levels of the body. This arrest could be appreciated by observing the degree of development of the similar organs on the opposite side of the body which were apparently normal. Miss Brown suggests that these developmental disturbances were possibly associated with aberrant vascular development.

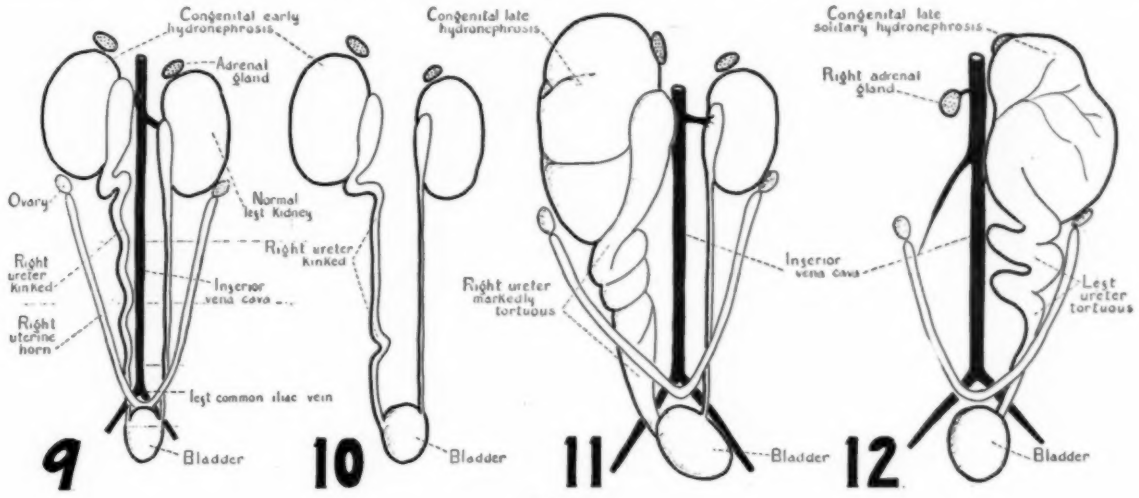

PLATE II.

FIGS. 9–12. Progressive degrees of congenital hydronephrosis.

I suggest that in addition to the above-mentioned condition of relatively early developmental arrest of kidney growth, one or both kidneys may be caused to disappear at a relatively late stage of gestation. In fact this suppression may be instituted at intervening points between the two extremes. My suggestions are based on the study of 1000 animals with one or both kidneys missing at birth, in which congenital hydronephrosis was noted in 48 instances. My observations suggest that there is a relation between congenital hydronephrosis and the solitary

[2] *Anat. Rec.*, 38:5, 1928.

kidney condition. Plate I has been prepared to illustrate by graphic means various stages in this process. Figure 1 shows two kidney remnant keeps its relative position in the body in relation to the other kidney. Early congenital hydronephrosis is shown

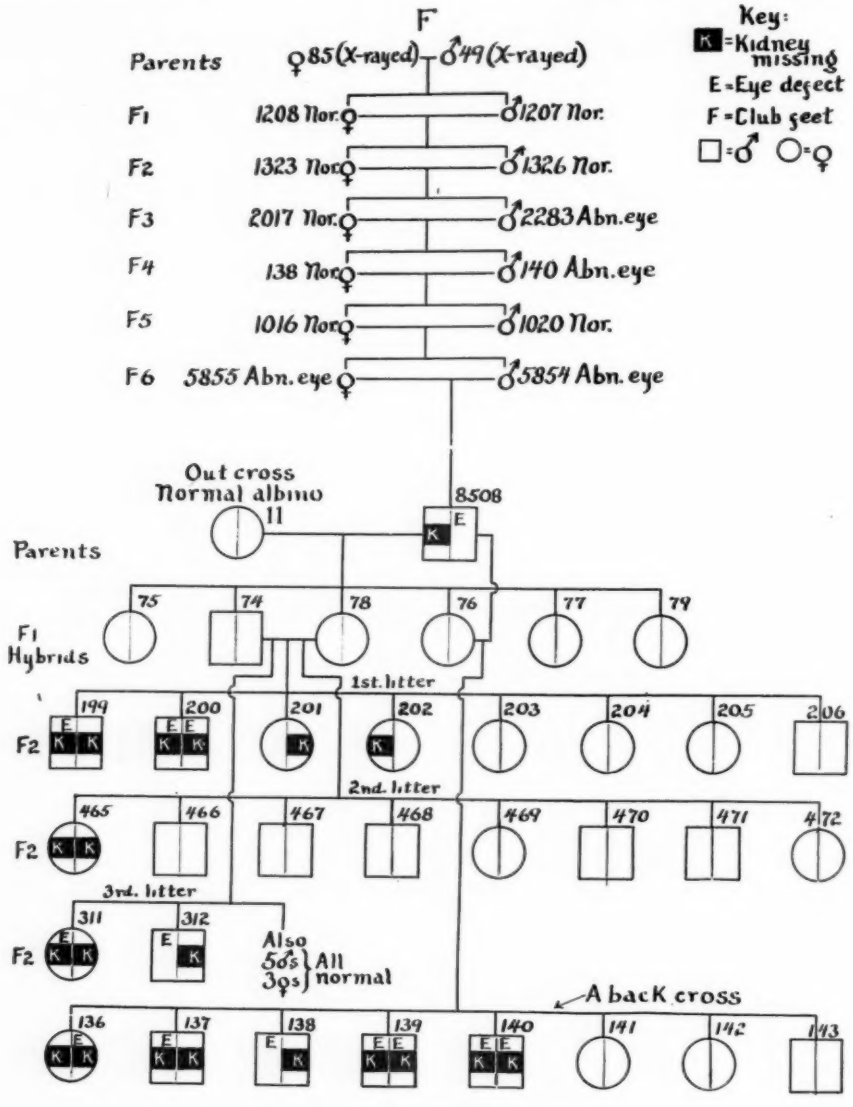

PLATE III.

FIG. 13. Pedigree chart showing immediate ancestors of male, No. 8508, used as a parent in an out-cross mating with normal albino female, No. 11. Note that roentgen rays were given only to two animals of parent generation. First-generation hybrids were all normal. Their *inter se* matings are here shown, and one back-cross mating which illustrates association of kidney and eye defects. Note symbols: squares, males; circles, females, are divided by vertical line. This line is drawn to represent mid-dorsal line of body dividing right and left sides. Thus No. 199 is male, blind in left eye and with both kidneys missing.

normal kidneys as seen from a ventral view, their ureters, the bladder and the two adrenal glands. Figure 2 shows the relative degree to which suppression of one kidney may take place without its complete disappearance. Note that the adrenal gland on the side with the small in Figure 3. Note the increase in size of one kidney, with the anterior displacement of the adjacent adrenal gland, and the distention of the ureter with its beginning tortuosity. Figure 4 shows a still later stage of congenital hydronephrosis. The kidney is now a very thin-walled, trans-

parent sac, the hydro-ureter is markedly tortuous and its pressure on the bladder has tended partially to displace that organ towards the opposite side of the body. If the advanced hydronephrotic kidney illustrated in Figure 4 should be partially absorbed, or if the internal pressure within the organ should become sufficiently great to rupture its delicate embryonic tissues, then a condition similar to that illustrated

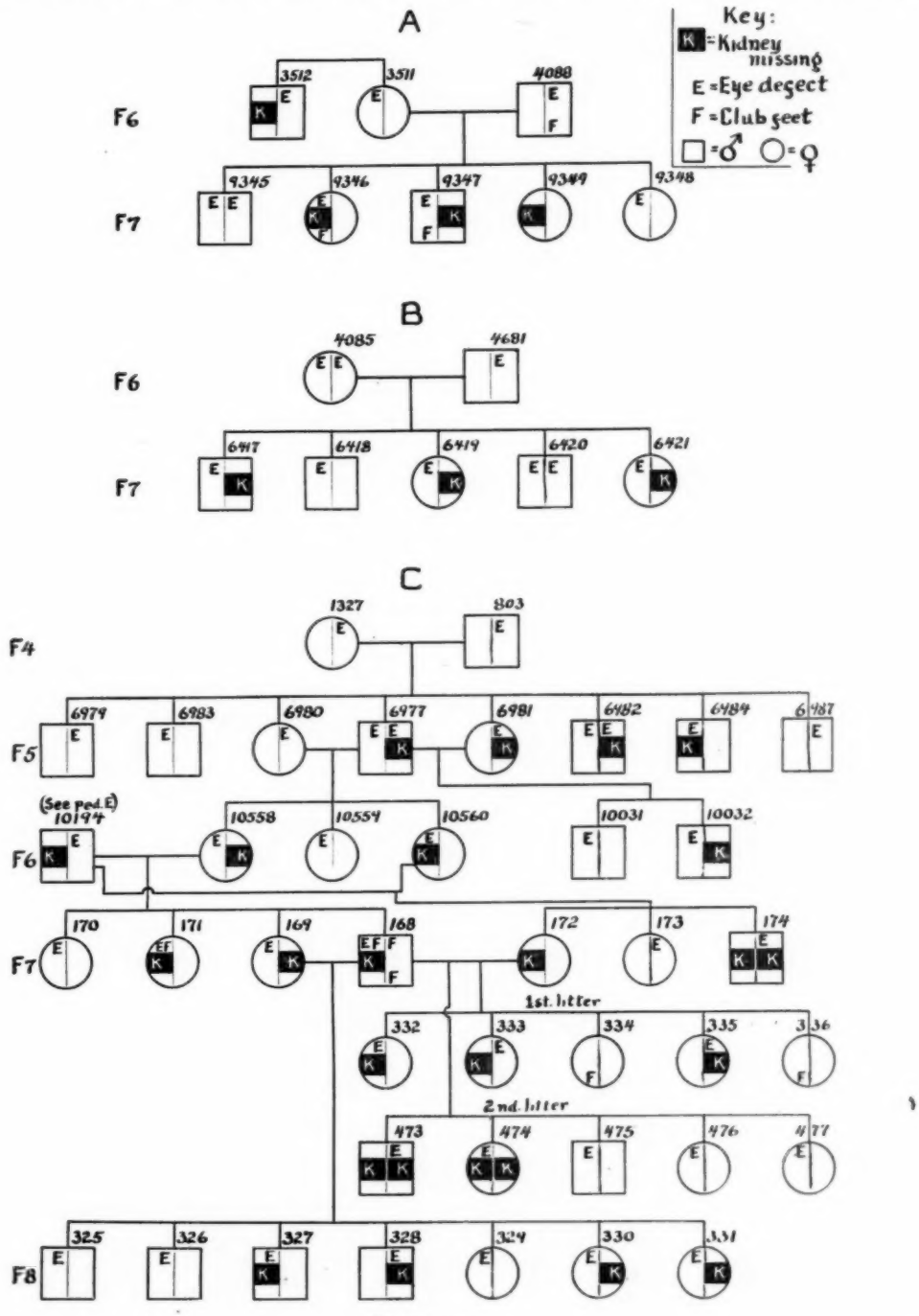

Plate IV.

Fig. 14. Pedigrees A and B show sixth and seventh generation animals with various combinations of kidney, eye and foot defects.

Fig. 15. Pedigree C shows various matings of animals with kidney abnormalities and resulting litters.

in Figure 5 would occur. This figure shows a normal kidney on one side of the body and the remnant of an absorbing hydronephrotic kidney on the other. Two such animals were actually found. They were killed at birth, placed in physiological saline solution and immediately studied under the binocular microscope. Thin, transparent, filmy tissues were found in the region of the missing kidneys respectively. It is our belief that this tissue represented the remains of absorbing hydronephrotic kidneys. Figure 6 illustrates the solitary kidney condition. Note that the ovary on the side of the body on which the missing kidney occurs is more medially placed than normal, and that the adjacent adrenal gland still persists. In fact, in all instances so far recorded (1057 kidney-defective animals) both adrenal glands have always been present and were apparently normal.

Figure 7 illustrates the only specimen so far recorded that shows bilateral hydronephrosis noted soon after birth. The kidney at the left of the figure shows an advanced stage of hydronephrosis, with a markedly distended kidney and tortuous hydroureter. The other kidney is in an early stage of hydronephrosis. It is interesting to note that this specimen shows a considerable amount of residual urine in the bladder. In order for this to happen at least one of the kidneys must have been functioning and discharging urine into the bladder at a time fairly near to parturition. This is evidence which shows that the disturbing factor producing hydronephrosis may make itself felt relatively late in gestation. Figure 8 illustrates the anephridic condition, showing both adrenal glands still present and also an empty bladder.

The four diagrams shown in Plate II, (Figs. 9 to 12 inclusive) were drawn from

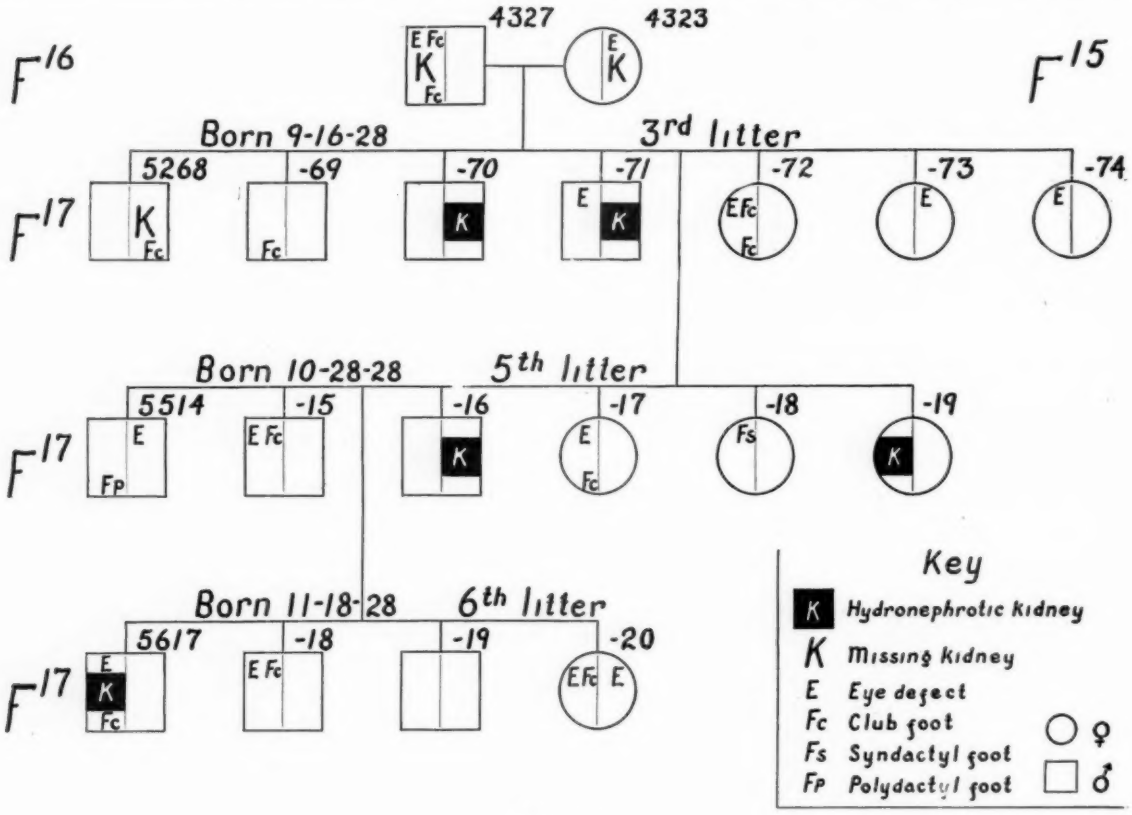

Plate v.

Fig. 16. Pedigree showing three litters of seventeenth generation, selected to show 5 hydronephrotic animals, offspring of pair shown at top of pedigree.

actual specimens and show from left to right increasing degrees of congenital hydronephrosis, with progressive increase in size of the kidneys with increased hydrodistention and tortuosity of the ureters. A study of serial sections of pelvices of hydronephrotic kidneys has shown that the blocking of the flow of urine is due to an occlusion of the ureter just superior to the vesicoureteral junction. The specimen

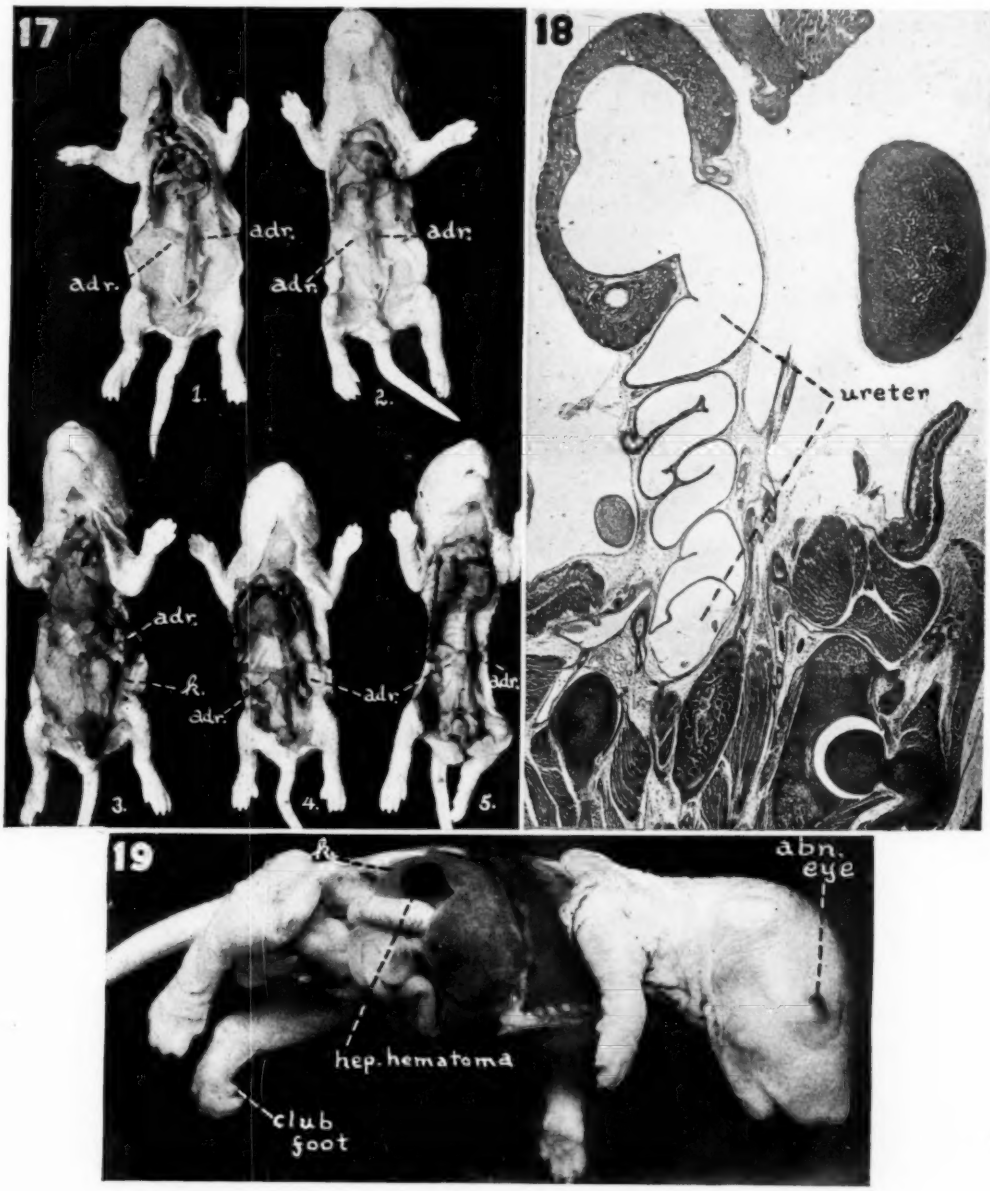

Plate vi.

Fig. 17. Five young of a single litter, seen from ventral view and with most of abdominal viscera removed. Nos. 1 and 2 were found dead twenty-four hours after birth. There was congenital absence of both kidneys in each animal. No. 3 is a male from same litter and shows normal kidneys. Nos. 4 and 5 were alive and well when killed about twenty-four hours after birth, but at autopsy were found to have no kidneys. Adr., adrenal gland; k., kidney.

Fig. 18. Microphotograph (low-power magnification) of renal and pelvic areas of an animal killed at birth with congenital hydronephrosis of right kidney. Greatly distended kidney shown at upper left of illustration, and to right is section of apparently normal left kidney. Note much distended and tortuous right ureter.

Fig. 19. Lateral view of day-old animal showing well-localized hematoma of right lobe of liver which presses directly on right kidney. Note abnormal eye and club-foot of left hind limb. K., right kidney.

in Figure 12 shows a solitary advanced hydronephrotic kidney. This suggests that the process which resulted in the obliteration of one kidney may have also produced the hydronephrotic condition in the other.

Certain hematomas have been noted at birth in the region where the ureter crosses the common iliac blood vessels. If a hematoma should appear here similar in magnitude to those so commonly found in the eye and foot regions in these same animals, then there would be a sufficient disturbing factor to account for the presence of ureteral occlusion as a result of this process alone. I suggest this explanation to account for possibly some of the hydronephrotic conditions I have noted.

It is possible that the suppression of a kidney may be due to extravasation of blood as a result of the rupture of the capillaries of the kidney itself. This is inference only and is based on the frequency of rupture in the capillary endings in the periocular and the digital regions and also in the testis and the liver in the same animal which has a solitary kidney.

The elimination of a testis after parturition has also been traced to diffuse hemorrhagic extravasation within that organ, which condition was noted a few hours after parturition and the same testis was missing at autopsy several months later.

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EXPERIMENTAL PRODUCTION OF EPITHELIAL HYPERPLASIA OF THE RENAL PELVIS*

GEORGE T. PACK, M.D. AND ROSS BUZZANCA, M.S.

NEW YORK BIRMINGHAM, ALA.

CHRONIC irritation is the most fruitful clinical and experimental source of cancer. Virchow strongly urged the theory of external irritation and Billroth predicated the trenchant assertion that without chronic inflammation there is no tumor. The wide varieties of chemical, mechanical and bacterial agents have nothing in common except the ability to exert a chronic tissue insult, therefore this quality is not specific. What potential tumor properties in cells are elicited by such chronic irritation? Is this cellular property a latent, inherent one, waiting for activation into neoplastic growth? Does the tissue stimulation by tar, pressure and other carcinogenic agents lead to prolonged cell proliferation, which in turn leads to cell variation of the specific cancer cell type? Does the chronic irritation produce a portal of entry for the theoretically ubiquitous cancer parasite? We do not know, but it is a significant fact that every cancer for which a predisposing cause is elicited, is related to some form of chronic injury. Ewing has said that chronic irritation is a very frequent exciting factor, even in those cancers explanable according to Cohnheim's theory.

The coexistence of salivary, pancreatic, biliary and renal calculi with cancers indigenous to these epithelial-lined channels is of more than coincidental significance to the student of cause and effect. Parker Syms found gallstones present in one hundred per cent of cases of primary cancer of the gall bladder and bile ducts. Bland-Sutton's statistics for the same combination are 95 per cent.

The same percentage of incidence does not obtain for calculi and neoplasms of the renal pelvis, but their association has been observed by urologist and pathologist. In the interpretation and evaluation of this fact, the following questions must be answered:

1. Is the association of calculi and neoplasms of the renal pelvis merely coincidental?

2. Does the renal stone irritate the pelvic mucosa sufficiently to evoke a neoplastic response?

3. Is the renal stone secondary to a pre-existing papillary or ulcerative tumor of the renal pelvis? Certainly a papillary tuft or shaggy ulcer offers an excellent nidus for the deposition of inorganic salts and colloidal matrix.

4. Is the stone the result of the same irritative factor which causes the epithelial proliferation, such as the presence of infection?

These questions may be answered by experiments. The surgical introduction of sterile pebbles into the normal kidney pelvis will eliminate coincidence, the disputed question of priority or antecedence of tumor over stone, and will exclude, for a time at least, the influence of infection.

EXPERIMENTAL PROCEDURE

Twenty-one healthy adult rabbits were anesthetized by ether inhalation. The left kidneys were exposed retroperitoneally through the lumbar approach. A small stab wound into the renal pelvis was made through the convex border of the kidney. Two or three rough sterile pebbles of uniform size were carefully introduced through this incision and directed by a probe into the renal calyces. A single silk suture sufficed to control the bleeding.

* From School of Medicine, University of Alabama, Tuscaloosa.
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Layer closure was performed; aseptic precautions were observed throughout each operation.

ney pelvis of the rabbit did not produce any grossly discernible injuries or constitutional effects. Thirty-five young rab-

Identification Number of Rabbit	Duration of Stones in Renal Pelvis	Weight of Kidney (Grams)	Hypertrophy or Atrophy	Pelvic Capacity (cu. cms.)	Hydronephrosis Left Kidney	Hyperplasia of Transitional Epithelium of Left Renal Pelvis	Papilloma of Left Renal Pelvis	Albuminuria	Reaction of Urine
A Left Kidney	177 Days	15.0	Normal	2.2	No	Yes	Yes	Yes	Alkaline
A Right Kidney		20.2	Hypertrophy	3.0					
B Left Kidney	173 Days	6.5	Atrophy	4.0	No	Yes	No	Yes	Alkaline
B Right Kidney		15.0	Hypertrophy	2.5					
C Left Kidney	173 Days	7.0	Atrophy	2.2	No	Yes	Yes	Yes	Acid
C Right Kidney		10.9	Hypertrophy	2.4					
D Left Kidney	173 Days	10.0	Atrophy	2.5	No	Yes	No	Yes	Alkaline
D Right Kidney		13.0	Hypertrophy	3.0					
E Left Kidney	166 Days	12.0	Normal	2.5	No	No	No	Yes	Alkaline
E Right Kidney		18.7	Hypertrophy	2.4					
F Left Kidney	166 Days	6.0	Atrophy	1.0	No	Yes	No	Yes	Acid
F Right Kidney		14.5	Hypertrophy	2.5					
G Left Kidney	159 Days	20.0	No. (Hydronephrosis)	8.5	Yes	No	No	Yes	Alkaline
G Right Kidney		12.0	Normal	2.2					
H Left Kidney	157 Days	4.5	Atrophy	1.0	No	No	No	Yes	Alkaline
H Right Kidney		18.5	Hypertrophy	2.5					
I Left Kidney	157 Days	3.5	Atrophy	1.0	No	No	No	Yes	Alkaline
I Right Kidney		16.0	Hypertrophy	3.0					
J Left Kidney	154 Days	2.0	Atrophy	0.7	No	Yes	No	Yes	Alkaline
J Right Kidney		11.0	Hypertrophy	2.0					
K Left Kidney	154 Days	3.0	Atrophy	1.0	No	Yes	No	Yes	Alkaline
K Right Kidney		16.5	Hypertrophy	3.0					
L Left Kidney	149 Days	7.5	Atrophy	2.0	No	Yes	Yes	Yes	Alkaline
L Right Kidney		18.0	Hypertrophy	3.2					
M Left Kidney	121 Days	10.0	Normal	1.5	No	No	No	Yes	Alkaline
M Right Kidney		13.5	Hypertrophy	2.5					
N Left Kidney	121 Days	4.5	Atrophy	2.0	No	Yes	No	Yes	Alkaline
N Right Kidney		15.0	Hypertrophy	3.0					
O Left Kidney	114 Days	4.5	Atrophy	1.5	No	No	No	Yes	Alkaline
O Right Kidney		15.0	Hypertrophy	3.0					
P Left Kidney	13 Days	Left Peri-Nephritic Abscess			No	No	No	Yes	Alkaline
P Right Kidney									
Q Left Kidney	107 Days	5.5	Atrophy	1.5	No	Yes	No	Yes	Alkaline
Q Right Kidney		10.0	Normal	2.5					
R Left Kidney	107 Days	4.0	Atrophy	1.0	No	Yes	No	Yes	Alkaline
R Right Kidney		10.5	Hypertrophy	2.5					
S Left Kidney	107 Days	25.0	Hydronephrosis	6.5	Yes	No	No	Yes	Alkaline
S Right Kidney		15.7	Hypertrophy	3.0					
T Left Kidney	100 Days	9.5	Normal	1.5	No	No	No	Yes	Alkaline
T Right Kidney		18.5	Hypertrophy	2.8					
U Left Kidney	84 Days	7.5	Atrophy	2.0	No	No	No	Yes	Alkaline
U Right Kidney		18.8	Hypertrophy	3.0					

Fig. 1. Table of experiments and results.

There was no immediate operative mortality. The only animal to die spontaneously was 1, which survived the operation for thirteen days; necropsy revealed a left perinephritic abscess. The operation and the presence of the pebbles in the kidbits were born in this rabbit warren from the date of operation to the time the mothers were killed for examination.

RESULTS

There were 2 instances of hydronephro-

sis of the intrarenal type. In rabbit G, three stones had been introduced into the left renal pelvis; in 159 days the left pelvic capacity was 8.5 cu. cm., as compared with the pelvic capacity of its companionate kidney, 2.2 cu. cm.; one stone was imbedded in the ureter below the ureteropelvic orifice, another was completely obstructing the ureter at the level of the pelvic brim, while the third and preceding stone had passed completely through the urinary passageways. In rabbit S, two stones had been introduced into the left renal pelvis; in 107 days the left pelvic capacity was 6.5 cu. cm. as compared with the pelvic capacity of its fellow kidney, 3 cu. cm.; one stone remained in situ, the other obstructed the ureter 1 inch above the ureterocystic junction; a left hydroureter was present. The calyces of both renal pelves were globular in outline. There was a consistent dilatation of the collecting tubules, especially near the central part of the papillae. The epithelium of the convoluted tubules had undergone degeneration and desquamation. The renal parenchyma was involved in an extensive replacement fibrosis. The glomeruli exhibited capsular fibrosis, and some hyalinization of the connective tissue type. It is pertinent here to recall that partial ureteral obstructions from calculi which were produced experimentally by feeding oxamid to rabbits have also led to hydronephrosis.

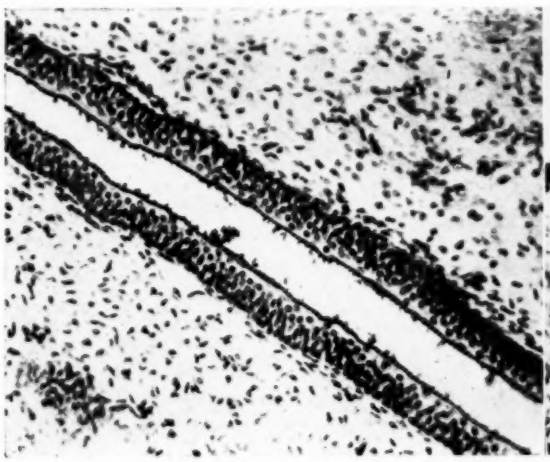

Fig. 2. Photomicrograph of normal kidney pelvis of rabbit (through calyx).

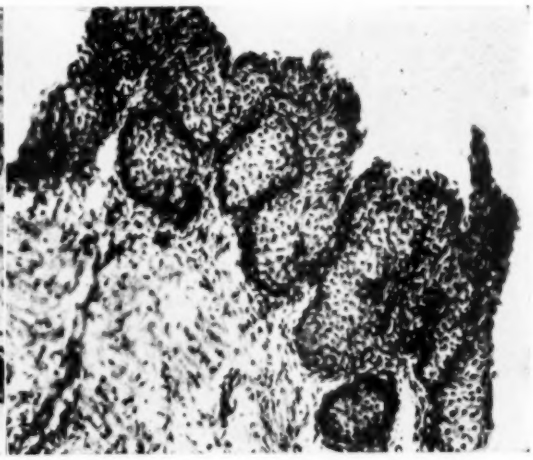

Fig. 3. Epithelial hyperplasia of tunica mucosa of renal pelvis of rab.

Of the remaining 18 pairs of kidneys, 14 gave evidence of definite left-sided atrophy and compensatory right-sided hypertrophy. The 7 of these left kidneys in which atrophy was quite marked and the number of stones introduced into each renal pelvis are as follows; H—2, I—3, J—2, K—2, N—2, O—2, R—2. (Fig. 1.) At the time of necropsy each of these seven kidneys lacked one of its alloted stones; a phenomenon which was not consistently found in those left kidneys, having no or less atrophy. The natural inference here is that the stones in transit produced a sudden and complete ureteral obstruction with subsequent elevation of intrapelvic pressure and eventual atrophy, as the older experiments of Cohnheim, Albarran and others have shown. The renal injury of operative origin was a uniform factor in all the changes observed in the left kidneys. The hypertrophy of the right kidneys is an anatomical response to a functional demand or emergency. Only a portion of the renal secretory units are actively and alternately functioning at any one time in the normal kidney, hence the great majority of glomeruli and tubules are at rest. With the incapacitation of one kidney, more of the renal secretory units are used in the remaining kidney; this results in individual enlargement, not numerical increase in the glomeruli and tubules of the hypertrophied kidney.

EPITHELIAL HYPERPLASIA OF THE RENAL PELVIS

In 50 per cent of the calculous pelves some degree of epithelial hyperplasia could be seen microscopically. In 3 instances, definite papillomatous hyperplasia occurred. The frequency of these interesting changes was in direct proportion to the number of days of residence of the stones in the renal pelvis.

Fig. 4.

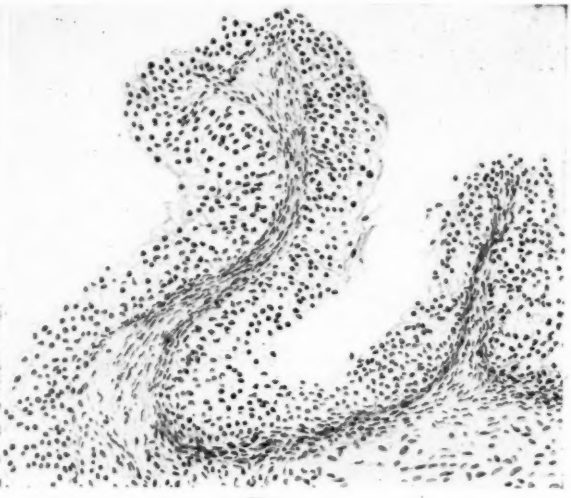

Fig. 5.

Figs. 4 and 5. Microscopic views of villous papillomata of the renal pelvis. Fig. 4 200/1; Fig. 3 250/1.

The normal tunica mucosa of the renal pelvis consists of several strata of cells (usually 4 to 8). This stratified epithelium is transitional in type and may be histologically differentiated into three distinct layers: (1) the innermost or surface zone in contact with the urine; these cells are either cuboidal or low columnar in type and are frequently flattened to a varied degree, with concave under surfaces into which the rounded ends of the intermediate cells project; (2) the intermediate cells, which are pyriform, conical or club-shaped; these have rounded internal extremities and narrow external extremities, that are wedged between the cells of the basal layer; (3) the basal cells, which are rounded, oval or irregularly columnar; they vary in number and present tiny anchoring fingers or processes extending into the basement membrane.

The hyperplasia observed was purely epithelial in type. It was more marked near the ureteropelvic orifices. The earliest evidence was the loss of structural integrity, particularly the substitution for the three previously mentioned layers, of an epithelial cloak consisting of cells of the basal type surmounted by many layers of cuboidal rounded cells, with clear cytoplasm and pycnotic nuclei. The outer zone of these hyperplastic areas never exhibited typical keratinization but did have some of the histological characteristics of squamous epithelium. Although the morphological transformation of this transitional epithelium is striking, the degree of change is insufficient to warrant the application of the term metaplasia. At most, we can say that due either to the changed environment of these cells or to the new and unaccustomed formative stimulus, i.e., the renal stones, a histological accomodation has occurred in step with the functional transformation of this kind of mucous membrane into a protective epithelium, of the same genetic order as its precursor.

"That the pelvic and ureteral epithelium is capable of extensive epidermization is well attested by the reports of Wendel of numerous cases of leucoplakia, usually associated with

calculi . . . Ziegler found marked epidermization in pyelitis calculosa and Beselin reported an advanced case with tuberculous pyelitis. Yet all cases are not associated with calculi or leucoplakia, so that the excessive hornification must be regarded as a tendency inherent in the growth." Ewing.[1]

The pelves containing the papillomatous changes were velvety and shaggy in gross appearance. With the magnification of a hand lens, the papilliform fronds were seen to occupy the regions near the pelvic outlets. The tunica propria of these three left renal pelves was the site of some round cell infiltration, edema and fibrosis. The previously mentioned hyperplasias were of the type that are commonly associated with stone or infection and were confined to the epithelial layer, whereas the papillomatous processes occurring in kidneys, A, C, and L, were tufted villous masses, containing a connective tissue core or stroma and capillary blood vessels. Here the injury has been deeper and the connective tissue has responded together with epithelial proliferation. Stoerk believes that injury to the renal pelvis is followed by regenerating fibrosis, which is the etiological factor in the development.[2] He declares that the large blood vessels grow up toward the surface, branch out and are eventually covered by an overgrowth of epithelium. Histological study of our specimens does not confirm this theory.

Many of the papillomas are covered with heaped-up epithelium, the cells of which are hydropic and vacuolated. Occasionally two nuclei are seen within one cell; this may be the result of amitotic or direct cell division, an unusual phenomenon that has been observed in the transitional epithelium of the renal pelvis. The surface epithelium is composed of flat, almost cornified cells, which have lost their nuclei and are constantly desquamating.

DISCUSSION

There is one point about the modus operandi of tissue-stimulating and carcinogenic substances, which is very helpful in explaining the difficulties awaiting the research worker. This has to do with the time or duration of action of the active agent. In the human, there is the probability that the production of many cancers is a very slow process, frequently comsuming ten to forty years, hence the cancer may not make its recognizable appearance until middle or old age. On the basis of relative longevity of rabbits and men, the residence of a stone in the renal pelvis of the rabbit for 177 days is equivalent to a computed duration of ten years in the human. Whereas simple hyperplasia occurred within 107 days after the known date of introduction of the stones, the benign villous papillomas first appeared after 149 days. The results of these experiments are as yet insufficient to justify the assumption that longer time would permit malignant transformations. In 108 cases of associated renal calculi and malignant disease of the renal pelvis, reviewed by Martin and Mertz,[3] the symptoms suggestive of cancer had been present about five months; the symptoms suggestive of stone averaged nineteen years in duration. This emphasizes the importance of the factor of time in the production of new growths of the renal pelvis.

Infection is admittedly apt to occur secondarily to those stones which arise spontaneously within the renal pelvis. Infection hastens ulceration of the mucosa and by itself may induce villous pyelitis. Under the heading, Granulomas of the Kidney Pelvis, Braasch and Hurley[4] discuss the occurrence of localized areas of hyperplasia, varying from minute granular patches in the mucosa to the so-called papillomatous proliferations. They state further: "Granulomas may be observed in the pelvic mucosa as a result of chronic irritation from stone long resident in the pelvis. With chronic pyelonephritis the granulomas may be more marked and the mucosal proliferation more predominant, a condition often called pyelitis granulosa.

Granulomas of the renal pelvis are dark red, bleed easily and often have papillomatous structure." The illustrations in their article show an overgrowth of fresh connective tissue quite similar to ordinary granulations; there was no epithelial hyperplasia. In our rabbits, the urine was alkaline but there was no constant urinary evidence of renal infection; the urine was usually clear and contained more desquamated cells than leucocytes. There was no grossly visible exudate within the renal pelves; microscopic studies were equally uniform in supporting our conclusion that infection did not play an important rôle in the production of these villous papillomas.

Stasis and increased fluid pressure within the ducts of many organs will stimulate the ductal epithelium to proliferate under pressure. Adair considers the factor of stagnation or secretory stasis as playing a very important part in the causation of mammary cancer. Ribbert ligated the ducts of salivary glands and secured epithelial proliferation of the cells lining these ducts. Cervical stenosis and pyometra are quite frequent findings in carcinoma of the body of the uterus. Pancreatic and prostatic stasis is under suspicion as influential in or contributory to the development of cancers of these organs. Our motive in reciting these examples was to introduce the postulation that urinary stasis in the renal pelvis and in the presence of an irritant such as a renal stone, may be an auxiliary factor in tumor genesis. The stone therefore, may act in two ways; first by irritation through direct contact, and second, by causing urinary stasis through occlusion of the pelvic orifice. In a series of case reports concerning the association of stone and tumor of the renal pelvis, and appended in the bibliography of this article, hydronephrosis is more frequently found than is generally supposed; it may be concomitant; it may be secondary to either stone, tumor or both; or it may be partially responsible for the excitation of tumor growth.

CLINICAL EPICRISIS

The clinician will appreciate that, given the ideal setting of chronic irritation and the presence of the elusive unknown factor x, the percentage of genuine tumors developing is very small. Stones constantly accompany gall-bladder cancer, but the reverse is not true. Nephrolithiasis is a common condition; fortunately carcinoma of the renal pelvis is so infrequent, that no urologist encounters many instances during his personal practice. To guess the incidence of renal pelvic cancers following the presence of stones would be a hazardous venture, but the percentage would undoubtedly be quite small. Nevertheless, the evidence presented in our experiments, suggests that simple epithelial hyperplasia is a frequent sequel; it is conceivable that such hyperplasia subsides after surgical removal of the offending stones. From the other viewpoint, 15 to 35 per cent of all tumors of the renal pelvis are associated with renal calculi, according to various statistics. There are probably several factors, among which the presence of rough kidney stones should be included.

The benign villous papillomas of the rabbit kidney pelvis produced by calculous irritation of the tunica mucosa is another type of response; histologically it resembles and may be identical with the condition known as villous pyelitis. It little matters whether the irritation be mechanical or bacterial in this instance, the epithelial proliferative response is the same.

CONCLUSIONS

1. The surgical introduction of sterile pebbles into the renal pelvis of experimental animals offers a new avenue for approaching the study of hydronephrosis and hyperplastic changes in the pelvic mucosa.

2. Hyperplasia of the transitional epithelium of the renal pelvis is a frequent and early response to the presence of renal stones.

3. Benign villous papillomas of the renal pelvis occasionally follow irritation

by renal stones; this occurs later than the more frequent simple epithelial hyperplasia.

4. Urinary stasis is suggested as one of the factors involved in tumor genesis within the renal pelvis.

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Authors' Note. We wish to express our thanks to A. L. Seale and R. Terhune for the technical assistance which they gave during the course of this investigation.

DISCUSSION

Dr. Edwin Beer: The investigation was very well carried out and the results very enlightening. The whole research in the laboratory and literature opens up many subjects for discussion. In the literature, too much emphasis has been placed upon irritation as a cause of leucoplakia in the bladder, ureter and kidney pelvis. Though some cases, perhaps many cases, are associated with stone and tuberculosis, I have seen numerous cases in which no irritation was present, and I am inclined to think that instead of being the result of irritation, it was a congenital malformation. However, it is perfectly possible that chronic irritation may lead to such a metaplastic chain. A similar condition occurs in the membrane of the gall bladder where it also may lead to the formation of tumors. The striking thing is the sharp limitation of the area of leucoplakia from the adjacent healthy or diseased, normal appearing mucous membrane. The pictures of papillary excrescences produced in this experiment resemble those seen in proliferative or papillomatous cystitis, and are probably an expression of chronic infection. A small section of mucous membrane showing such a papilloma cannot be used for diagnosis. The whole area must be studied so as to appreciate the process is not a neoplasia. Whether this can go on and produce real tumors or malignancies, no one really knows. In the renal pelvis, papillary growths though frequently associated with stones, are not by any means regularly associated with stones and the result of stones. In the last three or four tumors in the kidney pelvis that I have seen, there is no evidence of any previous or present lithiasis condition. That stones do not often produce these tumors is also evidenced by the fact that in hundreds of cases of kidney stone that I have looked after up to date, I have never had to remove the kidney which had harbored the stone, for subsequent papilloma or carcinoma. This is a standing argument against stones no matter how long they are in the kidney, being the cause of benign or malignant growths in the kidney pelvis.

Dr. Halsey J. Bagg: As one who has struggled with these experiments with animals for some time, I would like to make a few remarks. Do I understand rightly that the oldest animal lived 177 days after the operation? Did the animal die or did you kill it?

From my own experience in similar work, I should think that six months' stimulation would give about the type of reaction that you obtained. I certainly think the experimental approach is a very sound one and would bear repeating with a large number of animals. If you can keep your subject alive for one or two years after your operation, you might very well expect a more definite expression

of a neoplastic tendency of the epithelial growth. I know that it has been possible to keep guinea pigs alive for as long as nine to ten years. Dr. Stockard has kept some for about that time, and I think that with care a rabbit might live for at least three years or more.

Dr. B. S. Barringer: I cannot help but have an idea that Dr. Pack is on the right track as to many of these factors in the causation of carcinoma of the kidney, ureter, and bladder. We have not yet gotten them all together, by any means, but chronic irritation certainly seems to do something and every once in a while you get some data that apparently brings that out. A case that I cystoscoped fifteen years previously had a chronic and total retention of urine; nothing could be done for him and he had to be catheterized. He had a very cloudy urine and maintained that for fifteen years; at the end of that time the symptoms changed and I did a cystotomy on him, and all over his bladder were large patches of infiltrating squamous carcinoma.

I had a similar case of chronic retention of urine from a diverticulum which must have extended from the time the patient was at Harvard to the age of sixty-seven, when he died. He developed a carcinoma of the bladder one year before his death, and I cannot but think that irritation had some part in it.

In analine dye workers, if carcinoma develops it is only after a long exposure in the analine dye factories; and often the carcinoma does not occur until some time after the patient has left the factory. There must be some irritant in the urine which we do not appreciate or cannot isolate which causes the carcinoma.

Dr. George T. Pack (closing): I appreciate greatly the remarks and suggestions of Drs. Beer, Bagg and Barringer. The failure to discover tumors of the kidney pelvis at the time of operating for or subsequent to the removal of stones is not significant, because of the marked disparity in frequency of these two conditions. We are not reporting any instances of experimental cancer of the renal pelvis, only epithelial hyperplasia in interesting frequency. In a collective review of the literature, I have found almost 200 reported instances of the association of renal stones and cancer of the kidney pelvis. Before discarding the influence of kidney stone in any particular case of kidney tumor, the clinician should elicit all the information available concerning the history of renal colic; the partly responsible stone may have made its exit.

These experiments should be repeated and continued for a longer duration. I was obliged to sacrifice the animals because of a change in residence which would have necessitated transportation over a long distance. As Dr. Bagg has said, it is difficult to produce an experimental cancer in a short-lived animal within six months time. In an equal period of time (six months), we have succeeded in producing papilloma of the anus of the goat, but not actual carcinoma.

SARCOMA OF THE BLADDER*

JOSEPH F. MCCARTHY, M.D., F.A.C.S., C. TRAVERS STEPITA, M.D., AND S. J. HALPERIN, M.D.

NEW YORK

A STUDY of the literature on malignant tumors of the bladder reveals that sarcoma is relatively rare.

To corroborate this statement we can quote extensively from the writings of earlier authors. Of the malignant tumors of the bladder, Munwes estimates sarcomata to be 4.5 per cent. Out of 180 cases of bladder tumors, Geraghty found 2 cases of sarcomata. Albarran personally studied 80 cases of vesical malignancies, finding only 2 sarcomata. Watson found 52 sarcomata in 853 bladder tumors collected from the literature, while Gardner gathered 7 in 369 cases. Senftleben receives the credit for recording the first case of bladder sarcoma in 1861; this diagnosis was corroborated by Billroth. Only 1 case of sarcoma was found in the series of 262 cases treated at the Mayo Clinic in 1922. Of 159 cases of bladder malignancies noted in the records of the Post Graduate Hospital, 2 cases of sarcomata were found. Munwes in reviewing the literature up to 1910 collected 107 cases of sarcomata, and added 1 which he personally studied.

Since then the following cases have been reported:

Binney (1914), 1 case.
Harpster (1915), 1 case.
Gardner (1915), quoting from operative results of different surgeons, 3 cases (after 1910).
Mixter (1917), 2 cases.
Geraghty (1918), 2 cases.
Stein (1920), 1 case.
McKenna (1920), 1 case.
Scholl (1922), 1 case.
Lowen (1923), 1 case.
Smith (1925), 1 case.
Jamieson (1925), 1 case.
Caulk (1926), 1 case.
Cecil (1926), 1 case.
Parmenter (1927), 1 case.
Hager (1929), 1 case.

It is very evident in a review of the literature that such growths are decidedly infrequent. With our 2 cases noted in the records of the Post Graduate Hospital the number of sarcomata reported in the literature to our knowledge numbers 128.

Sarcoma of the bladder can occur at any age, but is more frequent in the first and after the fifth decade in life. Munwes reported 98 cases of bladder sarcoma, with 15 per cent occurring in children under ten years of age. Steinmetz reported 13 sarcomata in 32 bladder tumors in children, and Ropitshek 40 sarcomata in 97 bladder tumors. Deming in reviewing the literature on primary bladder tumors in the first decade of life, found out of 65 cases, 37 cases of sarcomata or 56.9 per cent, 24 occurring in males, and 13 in females. Bladder tumors occur more often in the male than in the female, the ratio being about 3.1, as noted from recorded cases in the literature.

The majority of bladder sarcomata are primary, but secondary sarcomata do occur, although rarely, and are usually derived from neighboring tissues. Munwes believes that melanosarcomata are by far the commonest of the secondary sarcomata in the bladder. Mandelbaum described 5 metastatic fibrosarcomata of the bladder, and 1 lymphosarcoma originating from the lymphoid follicles of the appendix.

Sarcomata of the bladder in young and old are rapid growing, and exceedingly malignant. In the early stages, according to Munwes, they are small, single, and fairly well localized in the submucosa. However, due to the rapidity and invasiveness of the growth, the latter may develop in two directions: (a) It may infiltrate the

* Submitted for publication December 6, 1928.

whole bladder wall and extend to the surrounding tissues, seminal vesicles, prostate, rectum in the male, and uterus in the female, without breaking through the mucosa. (b) It may grow toward the lumen in a bulky, irregular tumor mass, lifting up the mucosa, lessening the capacity of the lumen, without, however, breaking through the mucosa. A reactive proliferation of the overlying epithelium may set in, thereby simulating a fibro-epithelial sessile polyp. Due to the pressure, and lack of blood supply, the epithelium may eventually ulcerate with resulting cystitis and subsequent ascending pyelonephritis, but as noted from the literature, ulceration is rare.

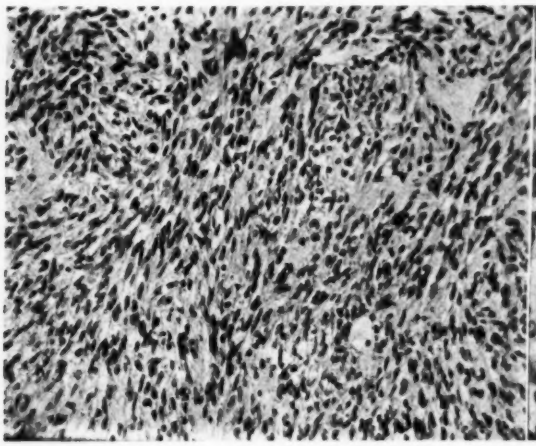

Fig. 1. Case 1. Low power photomicrograph, showing large spindle-shaped cells irregular in size and arrangement.

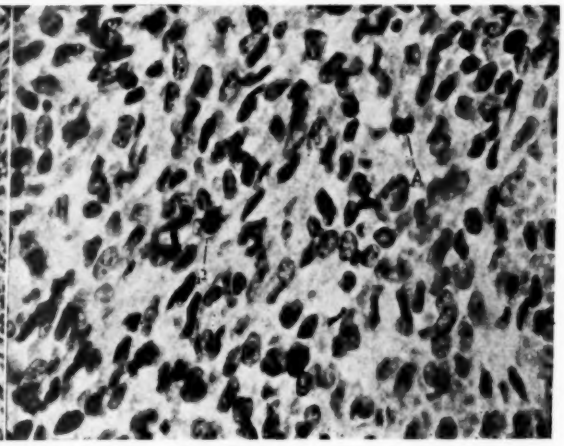

Fig. 2. Case 1. High power photomicrograph. Same spindle-shaped cells showing mitotic division forms at A and B.

As we have already mentioned, the tumor is primarily single in origin, but on account of the peculiarity of its growth, namely, the submucous mode of progress, with relatively late involvement of the mucosa and late symptomatology, as well as its enormously rapid development, it usually appears, at the time the diagnosis is made, as a multiple tumor, which has given rise to the impression among earlier writers of multiple origin. Many observers agree that this is due to regional metastases. The tumor is usually situated on the posterior and lateral walls. The trigone alone is not very often affected. The ureteral orifice may be encroached upon by the growth with resulting hydroureter and hydronephrosis.

Histologically, the types of primary sarcoma in this viscus may be:

1. Spindle cell sarcoma
2. Round cell sarcoma
3. Mixed cell sarcoma
4. Vascular myxosarcoma (Kaufman)
5. Osteochondrosarcoma (Beneke, Fischer)
6. Lymphosarcoma (Chaffey, probably metastatic)
7. Angiosarcoma (Jungano)

By far the commonest is the spindle cell sarcoma.

Early metastases are frequent, more often to the lungs and pleurae. Munwes stated that in 50 per cent of his collected cases metastases to different organs were found. Gardner collected 369 cases of bladder tumors, of which 7 sarcomata were operated on. Six out of 7 died shortly after operation; the seventh lived four years. Watson found 52 sarcomata in 653 collected bladder tumors; operation was performed in 35 sarcomata. Twenty-two (63 per cent) of the 35 died at the operation or immediately after. In 26 cases collected by Albarran, 13 patients (50 per cent) died as a result of operation; 10 had rapid recurrences or died shortly

after the operation. Munwes collected 107 cases; operation was performed in 69; 38 died soon after operation; only 3 were found to be free of recurrences, having been traced for five to thirteen years.

Surgical measures have proved unsatisfactory, probably due to the late diagnosis and rapid growth of the tumor, and in all the recorded cases, subsequently traced, death has resulted from uremia, septicopyemia and cachexia.

The principal and initial symptom is hematuria, which may come on suddenly and without pain. In the adult, hematuria is the initial symptom in over 75 per cent of cases. In children suffering from bladder tumors, hematuria is not an important symptom; the more frequent and important signs and symptoms are sudden retention or incontinence, with pain and tenesmus. The hematuria may vary from a blood-tinged urine to a profuse hemorrhage. It may stop for a time, only to reappear from hours to years later, often thus producing a sense of false security in the patient. The amount of hemorrhage is no indication of the size of the tumor. The hemorrhage may be painless at first, becoming painful only when clots are passed through the urethra.

Pain is the most inconstant symptom. It may be absent at first, later it may become severe and constant. Sarcomata near the urethral orifice are more painful than those farther away. The pain may be due to the accompanying cystitis, or to pressure of the growth on the pelvic nerves, in which case it may be referred along the course of the nerves. The pain due to cystitis is the most common.

Frequency of urination is another symptom, which may in many cases be the first indication of bladder trouble, especially in children. Obstruction of the urethra with resulting retention, and of the ureteral orifices with resulting hydronephrosis and pyonephrosis, may occur by extension of the growth. In females, on account of the shortness of the urethra, the tumor mass may be seen protruding from the urethral meatus. Cystoscopy and biopsy offer the only secure means of diagnosing bladder neoplasms, and should be the procedure

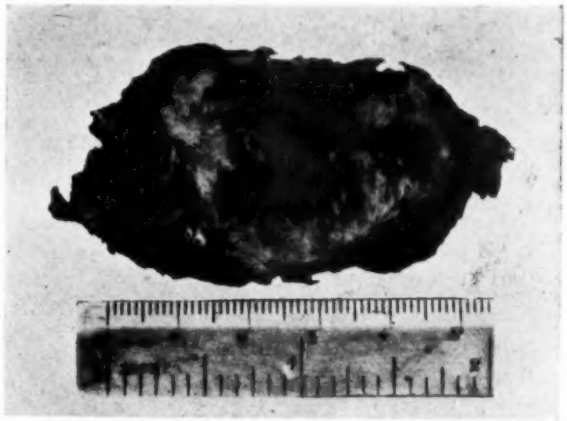

Fig. 3. Case 2. Cross section showing total tumor mass removed. Central portion necrotic as result of diathermy.

of choice in any case showing the above urinary disturbances.

To the cases of primary bladder sarcomata already recorded in the medical literature, we desire to add 2 cases observed in the New York Post Graduate Hospital.

Case 1. J. E., male, aged four years, was admitted to the hospital May 7, 1917, with history of dysuria for three months, being more marked at night, accompanied by frequency (every two hours) and voiding cloudy urine. The pain on urination was accompanied by priapism, and the stream interrupted several times.

Physical examination showed a well-nourished male child. Temperature on admission was 103.6°F.; pulse 96, and respiration 24. Eyes and ears: normal. Neck and chest: normal. Abdomen showed a palpable abdominal mass in left lower quadrant. Genitalia: penis semi-erectile. Rectal: negative as to palpation but pressure to left of prostate elicited pain. Urine examination showed, at different times, a cloudy or slightly bloody urine with moderate traces of albumin, few white and red blood cells. A provisional diagnosis of calculus was made, but roentgen ray was negative for stones. Blood count showed 22,000 white blood cells with 76 per cent polymorphonuclear leucocytes.

Cystoscopic examination revealed a markedly trabeculated bladder, with considerable internal

bulging at the left lateral wall. The trigone was congested. The right and left ureters were functioning. The urine from the bladder was hazy. There was no evidence of vesical calculi. Diagnosis of a low-grade cystitis and papilloma of the bladder was made. One week later, a suprapubic cystotomy was done. A large papillomatous mass was found, involving the greater portion of the bladder. Only a portion of the mass could be removed.

Fig. 4. Case 2. Low power photomicrograph showing intact mucosa with tumor taking origin in submucosa and its extent of infiltration.

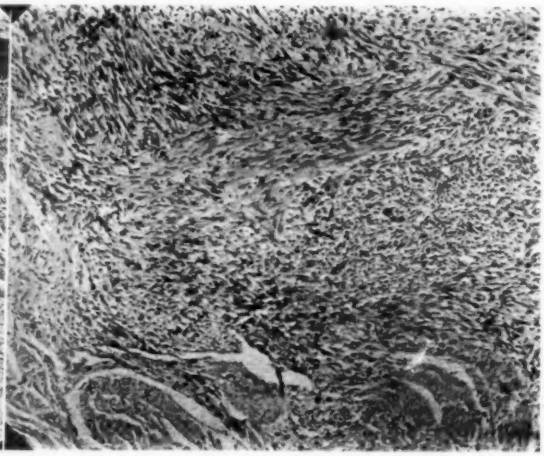

Fig. 5. Case 2. Low power photomicrograph showing extent of infiltration of tumor in deeper tissues, with only remnants of muscle tissue.

Patbological Report. Gross: Specimen consists of a number of irregular fragments, frequently hemorrhagic and having a colloid appearance (Fig. 1). *Microscopic:* The tissue fragments consist of an irregular mucosa of fibroblastic cells, which are of rather large type and frequently show mitotic dividing forms. The general appearance and character of these cells point to a neoplastic growth. They are, for the most part, spindle shaped, and do not contain much intercellular tissue. The blood vessels are poorly formed, and there are frequent focal hemorrhages.

Diagnosis. Spindle cell sarcoma. (Fig. 2.)

Treatment. Roentgen-ray treatments were applied with little improvement, for about one month after operation; a piece of redundant tissue was snared off from the wound, and the pathological report was that of a myxoma, bordering on a spindle cell sarcoma. The growth was very resistent to roentgen-ray treatments, and a large cauliflower mass was soon protruding from the lower edge of the wound. Patient died on September 13, 1917, after being four months in the hospital. Permission for autopsy was refused.

Case 11. J. G., male, colored, aged forty-eight years, was admitted to the hospital July 30, 1926 with burning micturition and voiding bloody urine and clots for one week before admission, accompanied by nocturia during that period. The patient did not know of any exciting cause. The hematuria at times was quite profuse.

Past History. Married. Five children, all dead, cause unknown. Had lues twenty-five years previously. Wassermann reaction had been negative for the last five years.

Pbysical examination revealed a well-nourished colored man. Head, chest, abdomen negative. Inguinal lymph nodes palpable. External genitalia negative. Urine examination showed at different times, moderate amount of protein, red and white cells. Roentgen-ray was negative for calculi. Wassermann reaction was negative. Blood count: 10,200 white blood cells, polymorphonuclear leucocytes 78 per cent.

Cystoscopic examination showed a cauliflower growth, posterior to the trigone, about the size of a half dollar, bleeding profusely. At that time the growth was diathermized. Trigone was regular, not elevated and injected. Bladder was intolerant. Some induration rectally.

Operation was performed on August 10, 1926, by Dr. J. F. McCarthy. Suprapubic incision. Bladder delivered extraperitoneally, opened and tumor mass plus about ½ inch of normal bladder wall, surrounding neoplasm, removed. Bladder closed with suprapubic drainage.

Pathological Report. (Fig. 3.) *Gross:* Specimen is bladder tissue, measuring 50 by 40 by 30 mm., with a large infiltrating tumor and a very small margin of healthy bladder tissue measuring from 6 to 9 mm. The center of the tumor is necrotic. On section, the entire bladder wall is infiltrated by a grayish white hemorrhagic tumor, which shows in its central part, a demarkated area 15 by 18 mm.

Microscopic. (Fig. 4.) Sections from the periphery of the bladder tissue show at the edges transitional epithelium. The stroma beneath is edematous and infiltrated with lymphocytes and a few polymorphonuclear leucocytes with dilated blood vessels. The entire wall is edematous. Approaching the center, the surface becomes denuded of epithelium and the underlying stroma formed by an arrangement of spindle cells with long spindle-shaped nuclei. Between the cells, there are numerous fibers. (Fig. 5.) The cells infiltrate the entire wall of the bladder and only a few remnants of smooth, muscular fibres can be found as shown by Von Gieson stain. In the subserous layer of the bladder, one can find a blood vessel with a plug composed of cells similar to those infiltrating the wall. The central area of tumor shows considerable necrosis but is composed of the same cells as described. Mitotic figures are quite frequent (Fig. 6). The tumor shows edema and infiltration with polymorphonuclear leucocytes, particularly in central areas.

Diagnosis. Spindle cell sarcoma of bladder.

September 27, 1926, bladder closed. September 29, 1926, pain in right hip. Roentgen ray negative for metastatic growth. October 3, 1926, patient was discharged in good condition and when last reported, eighteen months after leaving the hospital, was pursuing a useful occupation in good health.

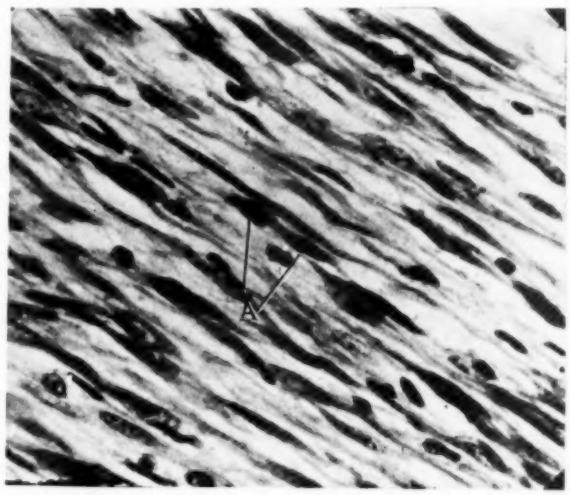

Fig. 6. Case 2. High power photomicrograph to show characteristic spindle-shaped cells with a mitotic figure at A (diaster).

SUMMARY

1. A short review of the literature of sarcoma of the bladder with regard to primary occurrence, incidence, age, symptomatology and pathology is given.

2. Two new cases of spindle cell sarcoma are added.

3. Our conclusions are in full accord with tables and statistics of previous writers.

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THE OPERATIVE TREATMENT OF RENAL LITHIASIS*

WILLIAM C. QUINBY, M.D., F.A.C.S.

BOSTON

THE importance of infection and stasis in the production of renal stone is today universally acknowledged. Other minor factors doubtless enter into the picture, but of these we are less certain. Cases of lithiasis occur in which the calculi are formed in a kidney quite sterile, as well as others in which, though infection is present, there is no demonstrable evidence of stasis except for that caused by the stone itself. But in the majority of instances infection and stasis are coexistent. The ideal therapy is, therefore. not only to remove the stone but also to do whatever is possible toward restoring normal conditions within the kidney; that is toward relieving the infection and stasis.

The majority opinion recognizes today the great destructiveness of a renal calculus; the postulate of Chute that the presence of a stone in the kidney presupposes the eventual destruction of that kidney being in general true. This destruction is also prone to be of insidious progress so that, though a patient is known to be the bearer of a renal calculus, his continued good health and freedom from discomfort over considerable periods of time often tend to lead both him and his medical attendant as well to pay but little heed to the real importance of the situation.

Our experience has led us to look upon every renal calculus as an important matter demanding correction by one means or another at the earliest time possible after the diagnosis is established. By this I do not mean to give the impression that I would advise operative removal of every renal calculus, for many of them are of such small size that they will eventually be passed spontaneously. Such stones because of their easy mobility are often those causing the most severe and persistent clinical symptoms. Immediate operation is also not necessary in those instances of stone of larger size in which the urine is sterile and no evidence of blocking of the kidney exists. But in such cases, though operation may be deferred, unless distinct contraindications on account of some other of the bodily systems is present, the stones should be removed at an early date. One still finds the opinion expressed that operation, though advisable for stones of ordinary size, should not be done in instances where the stone formation is extensive, often of the "coral calculus" or "giant calculus" type. My feeling is that this opinion is largely based on the results of the older type of operation, uncontrolled by roentgen ray and performed without adequate access to the kidney. Certainly the destructive power of such a large calculus, aside from the fact that it rarely causes obstruction, is just as great as that of the smaller form, and from its very size and extent, spread over a much wider area of kidney tissue. Therefore I do not consider that the size of a calculus makes any exception to the general rule that a stone in the kidney should be removed by operation as soon as convenient after the diagnosis is made if it be too large to be passed spontaneously.

The elements of infection and stasis unfortunately cannot be treated in so positive a manner as can the stone itself. As for infection in the kidney, this will frequently subside after the removal of the stone, in cases when this infection is slight and not of long duration. In other more severe instances, much help is afforded the kidney in throwing off the infection by a direct drainage of the organ

* From the Urological Clinic of the Peter Bent Brigham Hospital, Boston, Mass.
Read before The American Urological Association (New York Branch) Nov. 28, 1928.

through a tube which centers the pelvis by way of a nephrotomy opening. It is also very important in this regard that patients be seen after operation at frequent intervals in order to help the fight against infection by renal lavage in those cases showing positive culture of the urine. Also the whole patient must always be considered and earnest effort made to eradicate any existing focus of infection external to the urinary tract. Thus the ideal conduct of a case of renal lithiasis will consider the operative removal of the stone only an incident in the patient's entire surgical career.

As concerns the element of stasis after removal of the stone often but little can be done. In a large proportion of the cases of lithiasis there will be found present some form or other of developmental anomaly. We are all familiar with the kidney having a double pelvis or an intrarenal pelvis or those showing abnormal distribution of the renal blood vessels. Instances of unusual distribution of the renal mass are also common, such as come from faulty rotation or imperfect ascent of the organ. The various forms of renal fusion also fall into this group. All such conditions as these are prone to be associated with delayed motility of the calices, pelvis, or ureter and thus cause stasis, but it is only rarely that they are amenable to mechanical relief. Extraurinary conditions should always be considered if of such character as will interfere with renal drainage. An outstanding example of this sort is the involvement of the ureter in diseased retroperitoneal lymph nodes.

The aim of operation in cases of renal lithiasis should be to remove the stone and at the same time conserve as much renal tissue as is capable of function. For this reason a nephrectomy, though often an easier type of operation, should be done only as a last resort.

The delivery of stones from the kidney with as little trauma as possible to the organ, and the subsequent assurance that all stones and foreign material have in fact been removed, necessitates a very free mobilization of the organ and frequent use of the roentgen-ray film. Our experience has been that the best exposure is obtained through a transverse incision forward from the costovertebral angle to the outer edge of the rectus sheath. This incision will cross the course of the lower intercostal nerves, but these can easily be dissected backward from underneath the last ribs and need never be sacrificed. They will be found lying in the substance of the internal oblique muscle, and after being freed from the rib above can easily be made to lie out of the way alongside the inferior aspect of the wound. With the very free opening of the loin secured by this type of incision the kidney may readily be mobilized in a direction upward and inward about the axis formed by its vascular pedicle. In the presence of a high degree of induration and adhesion of the kidney to its fatty envelope, this will be a slow process often necessitating sharp dissec-

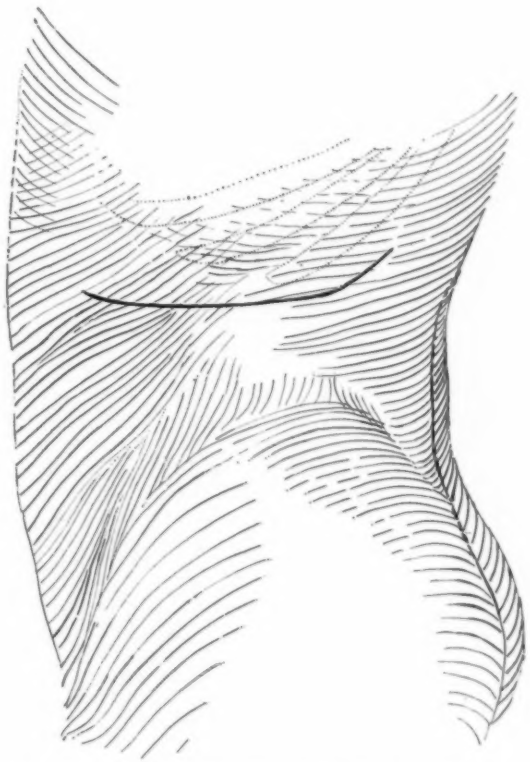

Fig. 1. Sketch of transverse subcostal incision.

tion, but if one uses care and persistence the organ can always be freed. A common anomaly which, when present, always

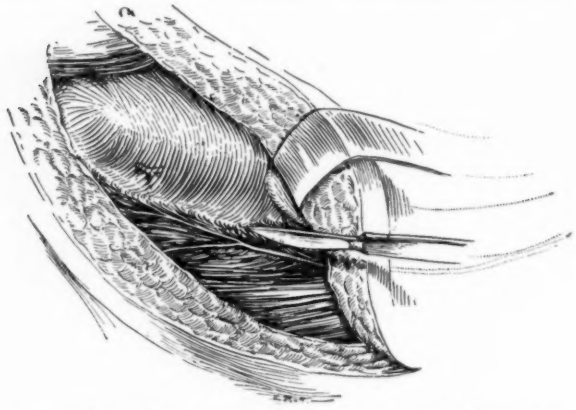

Fig. 2. Dissection of intercostal nerve away from its position underneath the rib.

By the time that the kidney has been mobilized there may be no doubt of the position of the stone and in such cases

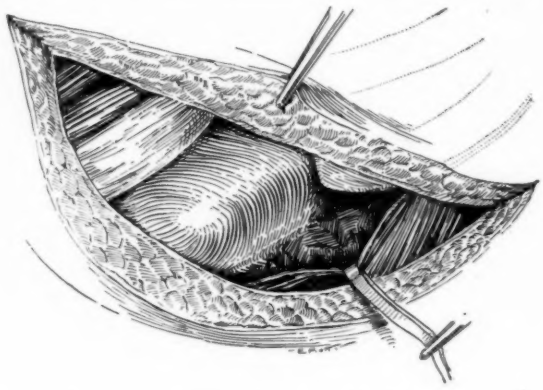

Fig. 3. Intercostal nerve freed and held downward out of field of operation by tape.

makes the delivery of the upper pole difficult, is an aberrant vessel. When short and of considerable caliber such a vessel may make it unwise to attempt to mobilize fully this portion of the organ, especially if the calculi are situated in other and more readily accessible areas.

The ureter is sought and surrounded with a bit of tape at a fairly early period in the process of freeing the kidney. By following it upward one is led directly to the renal pelvis which in normal instances lies behind the main vascular structures. In those instances where rotation of the kidney has been faulty the main pelvis may be found almost wholly below the vessels, or in cases of failure of ascent of the kidney, or in fusion, it lies anterior to them.

Having reached the pelvis its surface is examined for aberrant vessels and the first attempts are begun to palpate the calculus. One may at times gain considerable evidence concerning the position of a stone by palpating upward into the renal sinus. While the mobilization of the kidney has been underway, note will be made of areas of induration on its surface or of thickening and opacity of the capsule or of softening and thinning of the parenchyma. Such areas may often be found external to a calyx containing the stone.

one proceeds immediately to free it by whatever route seems best. The exact location of the stone may not be clear, however, and in such cases a roentgen-ray film is made immediately. With this at hand the problem is made clearly evident.

By far the easiest route through which to remove a calculus is that of the pyelotomy incision which, if it seems inadequate, may be extended a short way upward into the parenchyma. The majority of stones can be reached thus. Not infrequently a stone will be found to lie so far away from the main pelvis as to be inaccessible and we then employ a nephrotomy incision of such size as is needed. In cases of multiple stones I prefer multiple nephrotomy incisions to a single median section which, even when made, may not open that individual group of calices which must eventually be reached. Of recent years I find that I use this form of combined pyelonephrotomy more often than any other variety of approach.

All calculi which have become evident being removed, a roentgenogram is made to exclude the possibility of a calculus, or especially of renal sand, having been left behind. This I feel is the most important step in the whole operation. If sand is found it is removed by washing with salt solution or by the use of the negative pres-

sure tube ("sucker"). By this I mean a real negative pressure apparatus, such as is used in many types of operation, especially in brain cases, where it serves to remove blood from the surface. It is, as you all know, impossible to sponge the surface of the brain with gauze, for such a sponge acts as a microscopic curette. Profiting by this experience, we use the negative pressure tube to advantage in many instances. It sponges the depths of the wound, and relieves the field of bleeding so that we can see, in a better way than does gauze. In exploring a kidney we find it of great value, as one can very easily remove loose grumous material from a calyx which sometimes cannot be seen because it is not open. If after employing this method a few calculi remain behind, a continued search is made, until the kidney is entirely free. In all instances we should proceed until the final roentgen-ray film shows no such material in any portion. This combined procedure eventually serves to fulfill the aim of operation, namely, to free the kidney from all calculous material.

Because there is no doubt that calculi form on a nucleus of one kind or another, even though sometimes microscopic, we feel that all handling of the stone should be most gentle. We rarely apply forceps for purposes of delivery. We make instead an extra ½ in. incision in the parenchyma and deliver the stone by the use of the finger, rather than submit the surface of the stone to the abrasive effects of metal forceps. It is very easy indeed to scratch off a minute bit from the surface of a stone, which may, by chance, not be removed later.

Following operation, after we have ascertained that the kidney is definitely free, a suture is employed which, so far as the parenchyma is concerned, should be the underpinned suture so well described by Dr. Beer, usually with the use of fat to prevent cutting. The pelvis itself is always sutured. Also, in accordance with the degree of parenchymal destruction, I do or do not drain the pelvis by means of a tube through one of the nephrotomy wounds. I feel that one is less apt to make

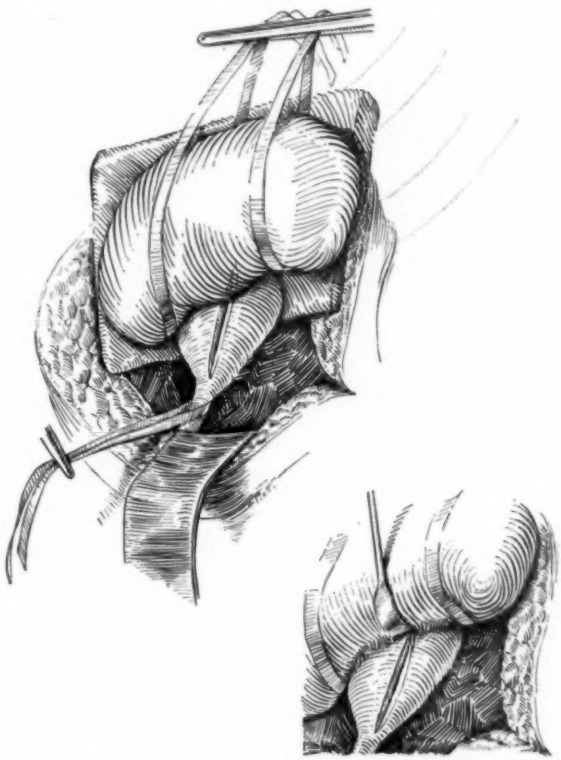

Fig. 4. Kidney fully mobilized. Flexible roentgen-ray film held against it preparatory to exposure. Inset figure shows how access to a higher point on the pelvis may be had by a retractor the tip of which is placed in the renal sinus.

a mistake by draining with a rubber tube through a nephrotomy wound than by not doing so. It certainly relieves postoperative intrarenal pressure, and helps to get rid of uncontrolled bleeding.

And in this respect it is important to mention that if there be definite bleeding points encountered during a nephrotomy, these should be treated by the application of fine tipped forceps and the use of the high-frequency current, or a definite ligature thrown around such bleeding points with a fine curved needle. The pelvis should be sewed loosely, before which, however, patency should be determined by passing an instrument all the way to the bladder. It is important in restoring the kidney to its fossa to see that it is firmly fixed, and that it is left in the best position for

drainage away from the organ. In other words, do not leave the kidney so lying in the wound that there will be tortuosities of the ureter.

As concerns recurrence of stone, I can tell you only this. We have been using roentgen ray at the operating table to be sure that the kidney is entirely free for only about four years, and have not yet investigated the results of this type of operation for comparison with those done before this period. I am firmly of the opinion that no statistics bearing on recurrence of renal calculi are of any value whatever unless supported by definite proof that the kidneys were freed at the time of operation. And the only way to determine this is by roentgen ray. Therefore, I feel that the old statistics on recurrence are absolutely without value.

In reviewing our statistics dealing with the various types of operations the following data as to relative frequency have been gathered:

In 226 cases no operation was performed in 10 per cent; nephrectomy was necessary in 11 per cent; and pyelotomy or pyelo-nephrotomy was done in 77 per cent. In these there was an operative mortality of three and one-half per cent. It is only fair to say that these 226 cases do not comprise all those observed, but only those admitted to the hospital. Some seen in the ambulatory clinic lacked sufficient evidence to warrant their entering the hospital. It is perhaps not a fair estimate, therefore, as it does not include all varieties of cases. Of these 226 cases the condition was bilateral in 8 per cent. I do not believe that the fact of a case being bilateral is of any special significance except that it makes a more definite appeal for operative relief.

CONCLUSIONS

1. In the absence of external contra-indications all renal calculi, which on account of their size cannot be passed through the normal channels, should be removed by operation.

2. Such operation should aim to remove the stone with as little destruction of renal tissue as possible, leaving the kidney so that free drainage is assured.

3. A free mobilization of the kidney, together with the use of roentgenograms made at the operating table, make it possible to appreciate clearly in every instance the problem presented and to meet it in whatever way seems best.

4. The simplest attack on the kidney is that of pyelotomy; the next most severe, pyelo-nephrotomy; the most severe, extensive nephrotomy. Nephrectomy should be performed only in those cases in which the kidney has been rendered valueless by the disease.

5. After all evident concretions have been removed, further search by roentgen ray should be made in order to be sure that no particles remain to serve as the nucleus of a subsequent stone. Such particles are best removed by washing and by the use of the negative pressure tube.

6. A final roentgenogram should show the kidney entirely free from shadow-casting material.

7. Patients should be closely followed after operation and every attempt made to restore their urinary passages to a sterile condition.

PHYSICAL THERAPY IN SKIN ULCERS*

HEINRICH F. WOLF, M.D.

NEW YORK

AN ulcer is a local necrosis of the skin. The etiology of this condition is manifold and the determination of the causes is very important for the prognosis and therapy.

Disregarding the etiology we can say that in each ulcer there exists an element of destruction and one of regeneration. The severity of the case depends on the prevalence of the destructive or regenerative factor, which again is dependent on the etiology.

It is very important to keep this fact before one as it determines what action we will take.

We can distinguish, in the main, the following causes:

Bacterial ulcers, i.e., syphilis, tuberculosis.

Trophic ulcers, i.e., after injuries or diseases of nerves, Raynaud's, bedsores. I include here roentgen and radium ulcers.

Circulatory ulcers, i.e., ulcus cruris, arteriosclerosis, thromboangiitis.

Burns.

Keeping in mind our conception of ulcers as the result of destructive and regenerative forces we direct our steps in such a way as to help the regenerative and fight the destructive forces. With some experience we can find the proper balance.

BACTERIAL ULCERS. In a syphilitic ulcer we have to deal with a destruction caused by the spirocheta pallida, in general, in a healthy individual. The regenerative force is active and for this reason, probably, we observe in such an ulcer the rolling edges.

The treatment consists in our effort to destroy the spirochete; if we succeed the regeneration takes place quickly.

In a tuberculous ulcer the destructive process is very active while the regenerative is very feeble. Whatever new tissue the organism may produce is quickly destroyed on account of the diminished resistance. The edges of the ulcer are worm-eaten, thin, undermined, cyanotic, unhealthy.

Local treatment is of very little value, in general it is harmful. It is obvious that with the destructive, local process overpowerful, any active treatment will in most cases add to the destruction. The treatment must consist in an endeavor to improve the condition of the entire system. Not a local but a general treatment is necessary. The splendid results of heliotherapy in combination with proper body hygiene are well known. With the improvement of the general condition the defences of the body are activated and the infection will be overcome.

TROPHIC ULCERS. In trophic ulcers we have to deal with a decrease of local resistance, due to various causes.

Following nerve lesions, e.g. myelitis, of various kinds the tissue becomes so vulnerable that the normal wear and tear leads to a local necrosis. The same may be said of bed sores which develop when the organism is weakened to such an extent that the slightest interference with the circulation caused by lying on these parts is sufficient to produce an ulcer.

Roentgen and radium rays destroy the vitality of the normal tissue and a necrosis develops. The surrounding tissue is also affected though to a lesser degree.

The procedure in these cases can be easily determined according to the introductory remarks.

It is obvious that in a trophic ulcer every effective stimulating modality must be harmful. Tissue which broke down without

* From the Department of Physical Therapy, Mt. Sinai Hospital, N. Y.
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apparent cause will not stand any additional strain. Gentle radiant heat with the accompanying improvement of the circulation is the only treatment which at least will do no harm. As is known, the results of local treatments are very unsatisfactory.

Bedsores will heal only if the pressure is relieved and the patient's general condition improved. Then a slight stimulation will be well borne and a treatment with an arc lamp which combines heat with ultraviolet rays gives the best results.

The great difficulty in the management of roentgen-ray and radium burns lies in the fact that the tissue surrounding the ulcer is very seriously injured, though not to the same degree as on the place where the ulcer developed. The results of treatments of any kind are very unsatisfactory, obviously because it is impossible to influence the floor and the neighborhood of the ulcer in just the right degree. We do too little or too much but is impossible to say beforehand what constitutes just enough. Whatever satisfactory results I have seen followed treatments with certain ointments and the air-cooled quartz lamp. The time interval between the beginning of the treatment and the first signs of improvement is so long that it is not certain whether one may attribute the change to the treatment or to the natural course of events. As long as we do not know how to restore the surrounding tissue to its normal vitality all treatments will be purely empirical and subject to doubt as to their efficacy.

Circulatory Ulcers. The discussion of the treatment of ulcers due to arteriosclerosis and thromboangiitis obliterans is bound up with the problem of handling these conditions and shall therefore not be taken up.

Ulcus cruris is due to a disturbance of the venous circulation. To suggest any form of treatment for a condition which in some cases heals after a few days' rest in bed, and in severe cases may even necessitate an amputation would hardly be logical. Likewise the modern method of treatment with pressure does not belong here.

Physical therapy is of great value in many cases but to use it successfully each case must be studied and its needs determined. The diagnosis ulcus cruris does not give any indication as to the method to be used. We must be able to understand what a given ulcer requires and we shall then be able to choose the modality which will be most likely to meet the requirements. Our procedure must accordingly be guided not by the diagnosis but by the reaction of the tissue which we want to bring about.

To elucidate this statement and report a few cases from my experience.

A woman came to the clinic with an old ulcus cruris. The surrounding tissue was indurated and showed the typical discoloration. The ulcer itself looked quite dry without granulation, a picture of inactivity. A course of treatment with the arc lamp had no effect. It was obvious that this form of treatment did not constitute a sufficient stimulation and that the tissue had to be whipped into activity. A few treatments with copper ionization changed the appearance quickly. Granulations developed, the wound became moist and showed tendencies to heal. The problem had changed. It would not have been advisable to destroy the healthy granulation with further ionization. The arc-lamp treatment was resumed again and the ulcer improved further.

In another woman we had to deal with an old ulcer covered with pus and sloughs. It was necessary first to destroy these unhealthy granulations with coppery ionization. Here the ionization had to be discontinued later after the original object was obtained, as the ulcer had become clean but did not heal. It needed a stimulation of the regenerative factor and not an assistance to the destructive one.

For an ulcer which shows tendencies of healing these tendencies should be favored. Ultraviolet rays in any form alternating with arc lamp or infrared rays to improve the circulation will be found of great value. The ultraviolet rays can be started with ten minutes, treatment, firstly be-

cause the strong pigmentation is a sufficient protection and secondly because the very object of treatment is stimulation.

In conclusion it can be said that the diagnosis of ulcer does not indicate which treatment might be effective. It is necessary to study the reaction of the tissue, the tendencies of the local process, the stage of the ulcer, the general condition of the patient and the etiology.

Burns. In dealing with burns we are confronted with a different problem. Here the cause of the destructive process has ceased to exist and the object is to enhance as much as possible the regeneration and to prevent impairment of function.

First degree burns may be disregarded.

Second degree burns consist in the formation of blisters. I may mention here that I have found from personal experience that it is possible to prevent or to minimize the development of blisters in the following manner. One should put ice on the injured part immediately. In this way one can decrease the hyperemia following the burning and thus prevent exudation. If the injury is not excessive this treatment is most likely to be successful. It is natural that once the blister has developed any such procedure may be useless or do harm. If the tissue is severely injured, the superficial circulation damaged, one cannot afford to decrease the circulation any further but must increase it.

Thus gentle heat, particularly from an infrared lamp, is most helpful. It is in such cases that bulbs emitting red light only are useful. The treatment should be continuous. It is test not to dress the wound as the removal of the bandage is very painful and the newly formed epidermis is taken off with the dressing. Under the steady heat the patients feel very comfortable and the healing is rapid. The heat can be applied continuously. Care must be taken to remove scabs if they form as they prevent the removal of secretion which causes fever from absorption. Ordinary incandescent lamps are not as good as they give a stinging sensation and cause discomfort.

In burns involving large areas special attention must be paid to the danger which lies in the formation of scars. Scars after third degree burns cause serious disabilities to joint motion. To avoid such disability at least partly it is necessary to allow healing in a position most favorable to function. In view of the danger of contractions by scar tissue, burns of the axilla must be allowed to heal in abduction, the flexor part of elbow in extension, etc.

ACUTE INTESTINAL OBSTRUCTION*

LEROY B. SHERRY, M.D.

LOS ANGELES

COLONEL Mattison, by his masterly exposition on intestinal obstruction its causes and diagnosis, has unwittingly aided me greatly in what is to follow. I am going to report no statistics. We all know that the mortality of acute intestinal obstruction lies anywhere between 20 per cent and 50 per cent when it should not be over 10 per cent. I am going to report no cases; unusual cases with brilliant results are interesting but of mighty little value.

Intestinal obstruction is ever with us; and I believe that the high mortality (and I say this advisedly), is of our own making due to the fact that it is always our desire to make out of each case the unusual; in other words, procrastination for the sake of diagnosis; for probably in no other condition is the time element of so great value. It is my firm conviction that a skeleton of diagnosis can be erected whereby it is possible to diagnosticate a condition, not a lesion, accurately enough to answer the paramount question: is interference necessary?

That then is my purpose. How well my scaffold will hold will soon be shown. The name intestinal obstruction is the term applied to a condition, not a lesion.

All Gaul was divided into three parts. Intestinal obstruction from the standpoint of (1) age incidence, (2) symptoms, (3) the lesion and its situation and (4) the treatment, may also be so divided.

AGE

1. Infancy. Intussception should be our first thought. Enterocolitis? Yes, but a previously healthy infant taken with acute abdominal pain, cramplike in character or suggesting a tumor mass in the abdomen, usually with an absence of the cecum in the right iliac fossa; with or without absolute constipation and blood and mucus in the stools, makes it obligatory upon the physician to prove that it is not an obstruction, any time from birth to the age of four; for fully 70 per cent of the cases occur before the age of two. Intussception first, then through the gamut of conditions that may simulate: simple colic, colitis, rectal polypi, prolapsed anus, peritonitis, etc.

2. Childhood, adolescence through to middle life. Acute abdominal pain, cramplike in character, associated with vomiting, with or without absolute constipation. Intestinal obstruction must be eliminated. This is the age of bands: operative, inflammatory or congenital; this and the next succeeding are the ages of strangulated hernia, the most common cause of intestinal obstruction and unfortunately the one that causes the highest mortality.

3. The last three decades of life. Carcinoma of the large bowel, whatever its situation from rectum to cecum; strangulated hernia.

SYMPTOMS

1. Pain. Acute abdominal pain, cramplike in character, unrelieved in six hours, signifies a surgical abdomen (excepting lead colic and food poisoning) the history will greatly aid in eliminating.

2. Vomiting. Late in low obstruction, early and severe in high. Constipation, early in low, late in high.

3. Shock. Some degree always accompanies.

And what of distention, absolute constipation, abdominal tenderness, fecal vomiting, visible peristalsis? But why wait that long? That should be the cry of the surgeon. Those are the cases he now receives. Why not give him a better chance?

* Read before the Los Angeles Surgical Society, November 16, 1928.

THE SITUATION OF THE LESION

1. Low in the large gut: Pain, cramplike in character, early and progressive distention, late vomiting, shock absent or of only moderate intensity.

2. Low in the small gut: Pain, more acute, usually centered about the umbilicus distention less marked, shock more severe, earlier vomiting.

3. High in the small gut: Pain agonizing in character, vomiting earlier and persistent, distention not present in the earlier stages. Shock intense.

TREATMENT

1. Emptying the distended bowel of its toxic contents. Early operation will obviate this, the most serious factor.

2. Release of the obstruction, if possible.

3. Systemic support of the patient and particularly the building up of the chlorides.

As great an authority as Moynihan says: "The suspicion of the surgeon should be on the alert and the probability—for it is no less—of the condition being a mechanical block of the intestine should be borne in mind." And further: "When the exact state of affairs is revealed on the operating table, it will constantly be found that precious time has been frittered away and that the operation, whether ultimately successful or not, has been performed too late."

Why are the vast majority of the cases of acute appendicits so readily recognized? Due simply to the caliber and courage of men such as J. B. Murphy who made "inflammation of the bowel" coroner's cases. In gunshot or stab wounds of the abdomen do we delay operation until we can absolutely diagnose a perforation? If we do we are too late.

Acute intestinal obstruction is one of the gravest of the abdominal catastrophies. Far better an abdominal incision with nothing found than that a remedial lesion should be allowed to progress to one inevitable end due to the desire for an accurate diagnosis of the lesion. I do not decry accurate diagnosis but I do decry the procrastination of diagnosis.

All causes of intestinal obstruction, other than those few that I have mentioned, comprise but 15 per cent and if we lost all of these, which we will not, our mortality would still be less than at present.

Am I destructive? Do I not see clearly enough that goal of all physicians, diagnosis? What method would I use?

1. Immediate attendance upon all cases complaining of acute abdominal pain.

2. As accurate a history as it is possible to obtain, not depending upon that taken by an interne, but rather that which is elicited by pertinent questions which experience has taught are of value: age, onset, previous health and operations, type and character of discomfort.

3. A physical examination, not that local to the part alone, but beginning from the head downward, for I do not believe that any man has a right to subject any individual to a surgical insult without this precaution.

4. I would eliminate, to my own satisfaction, the commoner things, as the hernial rings and the rectum.

5. The abdomen. Sitting down quietly and watching an abdomen ofttimes reveales more than any amount of palpation. Distention: is it local or general; is it upper or lower? Peristalsis: is it visible or suggestive with each spasm of pain? Scars. And then light palpation: this in itself will eliminate many of the commoner conditions such as tumor mass, abdominal rigidity or spasm, either local or general. Rigidity seldom occurs in intestinal obstruction except as a late manifestation; it is present early in hemorrhage, perforative or peritoneal irritation. It may be that a mass can be palpated, either sausage-shaped or indefinite. The abdomen may or may not be tender; tenderness is usually due to distention. Auscultation ofttimes aids when peristalsis cannot be made out.

6. I would examine the vomitus; its character, its odor.

7. The blood: leucocytosis.

8. The urine. Uremia can simulate intestinal obstruction. If it is suspected a blood chemistry is essential.

9. Enemata. One or two enemas in a short period of time are perfectly permissible, but I would constantly bear in mind the quantity the distal end of the gut may hold, and not be misled.

10. And lastly the roentgen ray, if it is available, for I believe that you will be convinced that a flat plate of the abdomen, properly interpreted, will be of untold aid.

And what of the dont's?

1. No attempt at catharsis. That is a diagnostic aid relegated to the past.

2. No bismuth meals; they give wonderful show pictures but hamper surgical emptying of the bowel to an untold degree.

3. Nothing by mouth; it will not be retained.

4. Morphia. Do not use it unless you are fully aware of the condition you are treating or have definitely made up your mind as to the procedure you are to follow. The false sense of security and well-being a hypodermic of morphine gives is often the direct cause of grave disaster.

And then, the signs and symptoms lead me to believe I am dealing with an obstruction of the bowel. Of all obstructions 85 per cent are due to hernia, bands or adhesions, carcinoma or intussception. Volvulus, tuberculosis stricture, gall-stone obstruction, mesenteric thrombosis, intussception in the aged and some of the rarer conditions are considered only in differential thinking.

My advice: immediate operation if it is within my power to bring it about, for the mortality is inversely to the length of time from the onset.

Possibly this is too academic; it may even be purile. My only purpose has been to bring out certain salient facts.

1. The mortality of acute intestinal obstruction is in our own hands; education of both the physician and laity.

2. Acute intestinal obstruction is a condition not a lesion.

3. The vast majority of the cases arise from known causes.

4. Age incidence has a direct bearing and should be constantly borne in mind.

5. The early symptoms are few but definite.

6. The treatment of mechanical obstruction is operative; its method in the hands of the individual surgeon.

7. Early operation is our only means of lowering the mortality.

FATAL PULMONARY EMBOLISM WITH SPECIAL REGARD TO PROPHYLACTIC MEASURES*

E. A. RYGH, A.M., M.D.

MINNEAPOLIS

CASE I. Mrs. E. H., aged twenty-nine, complained of "attacks of appendicitis" and indigestion extending back over a period of fifteen years, characterized by attacks of pain in the right lower quadrant and hiccoughing after meals. She had been married about five years, but had never been pregnant. Menses were regular, with some pain on the first day, and considerable backache. She had had a leucorrheal discharge for the past five years.

Physical examination: Weight 170 lbs., height 5 ft., 10 in., pulse rate 75, blood pressure, 130/80. Pyorrhea was present, but otherwise there were no abnormal findings in head, neck or chest. There was a small umbilical hernia, and tenderness and rigidity over McBurney's point. The Fallopian tubes were found to be enlarged and somewhat tender on bimanual examination.

Operation was performed the following day (Feb. 10, 1925). Under gas and ether anesthesia a retrocecal appendix was removed, adhesions between the chronically inflamed tubes and omentum broken up, and 2 ounces of olive oil poured into the pelvic cavity before closure. The tubes were not removed because they were patent and still functionally competent.

The patient seemed to be progressing favorably until about forty-eight hours after the operation when she became slightly irrational, the pulse became weak, there was definite cyanosis and dyspnea. This state of affairs continued for four hours; at this time she was pulseless, but seemed to breathe a little easier; about an hour later she died.

Necropsy showed infarction of the entire lower lobe of the right lung and a large embolic mass plugging the lower branch of the right pulmonary artery; and bilateral chronic salpingitis.

CASE II. Mrs. F. E., aged forty-two, complained of backache and excessive bleeding during her menstrual periods, dating back for about two years. There was also frequency of urination and constipation. She had been married twenty-three years, but had never been pregnant. Her appendix was removed when she was nineteen. She was in good health until her fortieth year when an attack of diplopia occurred, with cramps in the legs and numbness of the fingers. She was confined to bed for six weeks after this, and a physician diagnosed "autointoxication."

Physical examination: Weight 225 lbs., height 5 ft., 10½ in., pulse rate 100, blood pressure, 110/68. She was quite obese. There were no gross abnormalities in head, neck or chest. The abdomen was flabby, and a large firm mass was palpable in the lower abdomen, corresponding to the position of a pregnant uterus. On bimanual examination this was felt to be a tumor of the body of the uterus. There were large varicose veins in the lower extremities.

A subtotal hysterectomy was performed on Feb. 20, 1928, under nitrous oxide anesthesia. The uterus was about the size of a six months' pregnancy, and contained several large intramural fibroids. A cystic ovary was removed from the left side.

Her condition was reported as "good" immediately after the operation. On the third day she had a slight asthmatic attack, but seemed quite comfortable until the seventh postoperative day, when a stitch abscess developed. The next day she complained of pain in the rectum (hemorrhoids). On the twelfth day there was swelling and redness of the inner side of the left thigh and she complained of pain in the left thigh and leg. With this she developed fever (100.2°F.) of the septic type, rising a little higher each day until the nineteenth postoperative day, when, at 4:20 P.M. she had a very sudden attack of dyspnea, faintness and cyanosis. This continued with increasing severity, in spite of all efforts to revive her, and at 5 P.M. she died.

Necropsy was refused. However, the history and mode of death indicate clearly that death was due to embolism of one or more of the large pulmonary vessels.

* From the Bessesen Clinic. Submitted for publication January 11, 1929.

THE PROBLEM OF THROMBOSIS

Thrombosis of one of the larger veins of the body is the precursor of fatal pulmonary embolism. This dreaded complication presents a problem which must be attacked if surgical mortality is to be further reduced. According to Rowntree it was responsible for 9.6 per cent of the postoperative deaths at the Mayo Clinic in 1926; for more than 6 per cent of postoperative deaths in the past ten years, and for more than 7 per cent of the total postoperative deaths during the history of the clinic. These figures alone emphasize the significant part thrombosis and embolism play in postoperative mortality, and we may safely surmise that death from the same cause occurs as frequently, if not more frequently, in other clinics and hospitals.

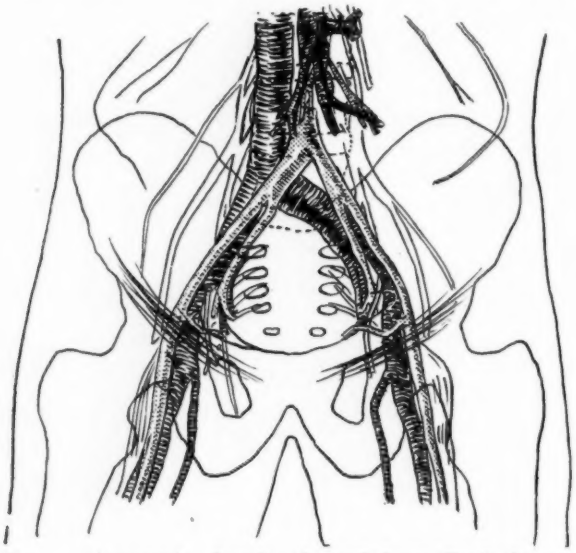

Fig. 1. Anatomic sketch adapted from Eycleshymer and Schoemaker demonstrates region of body anatomically most susceptible to thromboses. Here one may see left common iliac vein crossed by right common iliac artery; a little lower by left hypogastric artery; a little lower still is flexion caused by inguinal ligament. On left side of lower body is most fertile source of emboli. Unquestionably these anatomic factors produce variations in current of blood stream.

Obviously, since embolism is the end-result of thrombus formation, the problem can only be approached through a study of thrombosis. If the factor, or factors, which causes the formation of thrombi can be determined, prophylactic measures may be instituted.

In 1924, Aschoff, while lecturing in this country, discussed the thrombosis question from the pathological standpoint. He drew particular attention to the postoperative "spontaneous" thromboses which give rise to pulmonary embolism. In regard to the cause of the formation of these thrombi, he considered the following four factors:

1. Changes in the blood plasma (diminished or increased coagulability).

2. Changes in the blood elements (increased or diminished powers of agglutination). Aschoff described the white thrombus in its microscopic details, showing that its framework is made up, not of fibrin, but of innumerable platelets; the fibrin and leucocytes were only secondary.

3. Changes in the blood flow (slowing and formation of eddies). He further showed that the white thrombus was built up only in the flowing blood, but that this flow was a retarded flow. If there was absolute stagnation, as between two ligatures, no thrombus would form (Baumgarten).

4. Changes in the vessel wall (endothelial damage).

The physical and chemical characteristics of the blood plasma are profoundly altered by hemorrhage occuring during operations or delivery. Allen studied the blood changes in the ten days following operation, and found an almost 100 per cent increase in fibrin from the third day on, associated with a slight decrease in coagulation time most noticeable about the sixth day. In regard to the corpuscular elements of the blood, leukocytosis is a well-known occurrence after hemorrhage, due to concentration of the blood; but more interesting than this, when we recall the platelet structure of the white thrombus, are Ogata's observations in experimental anemia, in which he found a great increase in the number of platelets, coincident with the increase of giant cells in bone marrow and spleen, where they have their origin.

However, when we come to consider retardation of the blood flow, we have reached the *sine qua non* in the cause of thrombosis; it is without doubt the pre-

dominant factor. What conditions give rise to such a retarded flow? Some are constitutional, others local:

A. Constitutional conditions:

1. Weakened heart action and hypotension. This includes chronic myocarditis, secondary anemia, pernicious anemia, Addison's disease, traumatic shock, myasthenia gravis, adiposis dolorosa, and cachexia due to tuberculosis or malignant disease. Hypotension also accompanies most of the acute infectious diseases, being most noticeable at the height of the disease.
2. Obesity. These patients usually have a lowered vitality and a low metabolic rate.
3. Weakened vasomotor control. Toxemias due to focal infection, drugs, puerperal states, anaphylactic reactions, all have a tendency to produce a weakening of vascular tone.

B. Local conditions:

1. Pelvic stasis and vascular engorgement due to immobility of patientin bed and weight of abdominal viscera.
2. Anatomical relations of the pelvic vessels. The left iliac vein is crossed over by the right iliac, hypogastric, and middle sacral arteries, the femoral vein by the inguinal ligament, and pressure by these structures is accentuated when the patient is prone. When we recall that the great majority of large thrombi occur in the left iliac, the femoral, prostatic, and pelvic veins, it is evident that these peculiar anatomic relations tend to retard the blood flow in these veins, and thus predispose to thrombosis. Virchow called attention to these relations many years ago.
3. Varicosities. A varix is defined as "an enlarged and tortuous vein." Whenever a stream-bed widens, the velocity of that stream is lessened, other things being equal. The blood in the veins of the extremities is propelled toward the heart, not by the transmitted force of the heart beat itself, but by muscular contractions aided by the valves in the walls of the veins. Thus moderate exercise of the legs is essential in maintaining normal circulation. When we allow postoperative patients and convalescing mothers to lie in bed for a week or ten days practically immobile, as far as the pelvis and lower extremities are concerned, we are effectively blocking the normal circulation in these parts. When these patients are further hindered by the presence of varicosities in the limbs, the blood flow is materially retarded.
4. Infection. Thrombophlebitis is not the usual forerunner of the large thrombi which give rise to fatal pulmonary embolism, although it does occur most often in the same situations in which these thrombi arise. Aseptic surgery has not decreased the incidence of thrombosis. The consensus of opinion is that the infective thrombi are more likely to give rise to pyemia than to death by embolism.

Trauma to vessels resulting in endothelial damage is followed by an outpouring of fibrin and lymph, thus preparing the field for thrombosis. Vessels may be damaged during the course of an operation by roughness in handling tissues; the deep epigastric vein is no doubt often injured by too forcible and prolonged retraction, as was pointed out by Clark. The thrombus, once formed in this vein, rapidly extends to its junction with the external iliac. Similarly, the superficial epigastric vein may be injured and the thrombus extend into the sapheonous or femoral vein. The thrombus may occur on either side, or both, as there is free anastomosis between the epigastric veins; however, it is usually on the left side.

Hegler, commenting on the increase of thrombosis and embolism in Europe, has noted the occurrence of thrombosis several times in the same individual, as though there were a constitutional tendency to-

ward this condition. He also thinks there is a family tendency, several cases having occurred in two generations of the same family. Undernutrition, causing changes in the vascular endothelium and cell necrosis, he believes has been a predisposing factor in Europe. However, this can hardly be considered a general factor in our American statistics.

TREATMENT

Treatment must necessarily be almost entirely prophylactic, although a few daring operators have instituted what might be called active treatment by opening the thorax and removing the freshly arrived emboli from the pulmonary vessels. Recognizing circulatory stasis as perhaps the most important factor to be overcome in the prevention of thrombosis, various measures may be instituted in prophylactic treatment:

1. Weakened heart action and hypotension. Shock must be avoided by administration of fluids prior to operation, preliminary narcosis, careful choice and administration of anesthetic, keeping the patient warm, hemostasis, and gentle handling of tissues. In chronic myocarditis digitalization should be effected and foci of infection removed, as far as possible. In secondary anemia and cachexia, blood transfusion, forcing of fluids, and digitalis should be employed prior to operation.

2. Obesity. Walters administers desiccated thyroid prior to operation, in an effort to improve circulatory tone.

3. Weakened Vasomotor Control. Toxemias must be combatted by the use of fluids, ample nourishment, warmth, and drugs such as caffeine, epinephrine, and ephedrine. The use of drugs to raise the blood pressure and thus improve the general circulation is only a temporary expedient, but may be all that is needed in the first few postoperative days to quicken the flow and prevent thrombosis.

4. Pelvic Stasis. After any abdominal operation the patient is usually kept very quiet for the first week, and sometimes is kept in Fowler's position longer than may be necessary. This immobility, added to the weight of the abdominal viscera on the pelvic vessels, is bound to result in vascular engorgement and a retarded blood flow in those vessels. Coffey recommends deep breathing after these operations, and we believe that absolute quiet should not be insisted upon. The patient should be allowed to turn from side to side, and with proper closure of the abdominal wound there is little danger of its opening. The Lennander position (limbs elevated, body flat) is a help in preventing pelvic stasis.

5. Varicosities. Varicose veins should be eradicated prior to operation, either by excision, or by the modern and better method of injection of sclerosing solutions.

6. Infection. The possibility of a large embolus forming from a thrombus in an infected vein (usually left saphenous, iliac, or femoral) must be borne in mind. Here again, the vein which is the favorite seat of trouble is the varicose vein. Prophylactic treatment will therefore be directed toward obliteration of the larger varicosities. Granting the possibility of infection attacking the vein through a periphlebitis, rigid aseptic precautions should be taken in all pelvic operations.

7. Endothelial Damage. Roughness in handling tissues and too strong and prolonged retraction of the abdominal wall must be avoided, or we increase the chances of thrombus formation in epigastric, femoral, or deep pelvic veins.

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SURGICAL DIATHERMY IN MALIGNANCY*

G. KOLISCHER, M.D.

CHICAGO

THE relation of surgical diathermy to cancer therapy may be considered from the technical and scientific clinical aspect.

The technical advantages of using heat produced by high frequency currents for the destruction of malignant tumors were so frequently discussed that it will suffice to enumerate some of the most significant points of superiority of this method over the employment of the actual cautery.

The destructive heat may be applied at any point chosen, surgical diathermy guarantees an orderly procedure of the operation, and the extent of coagulation is fully under the control of the operator.

Incidentally it may be mentioned that the employment of the cutting current for partial or complete excision of malignant tumors provides a rapid severing of the tissues with a decidedly reduced hemorrhage and in most instances is painless.

The coordinate consideration of diathermic clinical results and of modern physiologic conceptions furnished a powerful impulse toward the emancipation of our reasoning from traditional concepts and to guide it into new channels of thought.

It was repeatedly observed that the only partial electrocoagulation of malignant tumors was followed by a complete cure. It was also noticed that in several instances of apparently complete destruction of such tumors accompanied by regional glaudular involvement, in the course of healing the glandular swellings disappeared, although those were not included in the surgical intervention. In this consideration are counted only enlarged glands that showed no sign of inflammation, so that they may have been with great probability diagnosed as malignant intumescences.

It was also observed that after the diathermic destruction of vesical tumors histologically identified as malignant, in several instances though no malignant recurrence was to be found, benign papillomata appeared after some length of time. The benign character of these growths was not only established by the cystoscopic examination, but also by the fact, that after cystoscopic fulguration these papillomata did not recur.

Through biopsy and post-mortem findings it was ascertained that in the zone of reaction around the area of coagulation there was always found an abundance of macrophages the defensive cells par excellence of the reticulo-endothelial system.

It is also a common experience that each repeated individual coagulation for malignant recurrences is promptly followed by an improvement of the general condition of the patient.

All these items point at the importance of systematic reaction as a factor that influences the possible succession of therapeutic intervention in malignancy.

A similar trend of reasoning is also indulged in by some radiologists who consider the systemic reaction produced by raying as at least of the same dignity as the direct destruction of the cells constituting a malignant tumor. An item in point is an observation that occasionally is to be made in cases of multiple lymphogranuloma.

In cases that are amenable at all the raying of one tumor only may lead to a disappearance of all the lymphomata. In such instances the systematic curative reaction certainly must have the superiority over the direct destruction brought about by the therapeutic rays.

The tendency toward appreciation of systemic reactions in connection with malignancy was bound to influence also

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the reasoning concerning the etiology of malignant tumors. So far there is no evidence produced supporting the supposition that malignant tumors are produced by the invasion of the body by foreign organized elements. Therefore the solution of this problem must be sought in other directions. There is no reason to believe that the cells constituting a malignant tumor should not be subservient to the same physiologic and biologic laws that govern the cells of normal structures. The production differentiation and aggregation of the somatic cells are obviously under the influence of opposing forces, of a stimulating and of a regulating character. It may be suggested that the unlimited proliferation and the invasion by malignant cells of other structures may be excited by a disturbance of the balance between stimulation and regulation in favor of the stimulation. It may be remembered that regions in which functional activity necessitates a forced reproduction of cells, form a site of predilection for malignant tumors as for instance the narrows of the intestinal tract.

That constitutional conditions have something to do with the development of malignant tumors is made plausible by other observations.

Chemical or mechanical irritations that are supposed to favor the appearance of cancers on certain areas antecede the tumors in a minority of individuals only, while other persons exposed to the same irritations remain free of such growths.

As a rule cervical cancers will luxuriate during pregnancy, but there are also cases on record in which an existing cervical cancer became pronouncedly reduced during gravidity. It seems more plausible to believe that the production of cancer is rather caused by a multiplicity of factors than to assume that there is only one generating influence.

The assertion may become reasonable that a cancer is even in its initial stages never a localized affair, but only the local manifestation of a general disorder, a misproportion of the stimulating and regulating somatic forces.

In harmony with this conception is the view of some pathologists who doubt that for instance cancer is due to a transformation of epithelial cells. They maintain that cells once highly differentiated become fixed in their specialization and cannot be transformed. They maintain that the cells aggregating into a malignant tumor are the product of the stimulation of the undifferentiated cells forming the reticulum around the capillaries.

In applying this reasoning to the cancer therapy it becomes evident that the direct destruction or excision of the tumefaction is only part of a successful therapeutic effort. Additionally the natural defensive forces of the body must be reënforced.

It is obvious that even if the operator should have succeeded in removing in its entirety the malignant tissues as they present themselves, no guarantee against recurrences is furnished, because the operation per se did not do away with the causes of cancer formation.

In summing up it may be said that surgical diathermy in malignant tumors not only possesses decided technical advantages but also provides one of the stepping stones for arriving at a chemotherapy of malignancy by furnishing excellent material for the further study of the systemic reactions determining the fate of malignant tumors and with that the fate of the carriers of such.

TREATMENT OF FRACTURES OF THE FEMUR BY THE HAMILTON RUSSELL METHOD OF TRACTION*

I. O. RIDGELY, M.D., F.A.C.S., AND H. F. BONGARDT, M.D., F.A.C.S.

BALTIMORE

IN any attempt at restoration of the loss of continuity of the bony frame of the thigh, one must bear in mind the individual forces which result as a consequence of the disintegration of the femur. A proper alignment of the fragments of the bone is a fundamental requisite for securing a successful issue in the treatment of any fracture, and this alignment must be maintained without interfering with the natural process of bone repair.

In the treatment of fractures of the femur two general classes of treatment have obtained. In the method of external fixation, plaster or some form of splint is used to choke the action of the muscles. In the second or internal fixation the forces which are active to bring about a malposition are resisted by fixing the fragment ends in some mechanical way. In either case approximation of fragment ends must first be secured.

Manual reduction under ether in complicated and in most simple fractures of the femur results usually in failure. Skin traction with the extreme pull required in adults invariably produces a skin lesion at the very site which must often be selected subsequently as an operative field. Skeletal traction requires an open operation and that method is limited in its application and in the hands of not a few has been scarcely uneventful. Should a successful reduction result many objections are still present.

A plaster spica is indeed a trial for a patient and actually does not immobilize. Such fixation as plaster does produce is obtained at the expense of pressure. The pressure results in some limitation of blood supply. It must accordingly delay the natural process of bone regeneration. The hip and ankle, and particularly the knee must be fixed for a long period resulting in such articular change that function of the joint is impaired much beyond the time at which weight bearing is permitted. The non use of the extremity results in a lessened blood supply.

Internal fixation presents many detrimental if not actively dangerous features. A simple fracture is converted into a compound one, a large area of periosteum is deprived of its circulation, a foreign body is introduced, and no very secure fixation of the united long axis of the bone is obtained.

Hamilton Russell described a method which is based not on external or internal fixation but depends entirely on neutralizing the forces of muscle elasticity which tend to force the fragments out of alignment.[1] This method requires no fixation; the fragments are passively immobilized in that there is no force active to dislodge them. The method in no way lessens the blood supply at the site of fracture. Increased activity of the muscles of the thigh increases the blood supply to the extremity.

To briefly review in a general way the anatomy of the thigh, with the exception of the adductor muscles, the larger muscles of the thigh have their attachment to the pelvis at one end and to the tibia at the other (Fig. 1). This is likewise true of the heavy fascial band which envelopes the thigh. By exerting a pull on the leg from the knee downward the forces are overcome which are active to produce shortening of the leg. The adductor muscles

[1] Russell, R. H. Fracture of femur. *Brit. J. Surg.*, 11: 491, 1924.

* Cases treated in Dr. Alexius McGlannan's Clinic, Mercy Hospital, Baltimore. Read before the Medical and Chirurgical Faculty of the State of Maryland.

are inserted into the linea aspera (Fig. 2). The function of this group of muscles is adduction and slight rotation. Accordingly

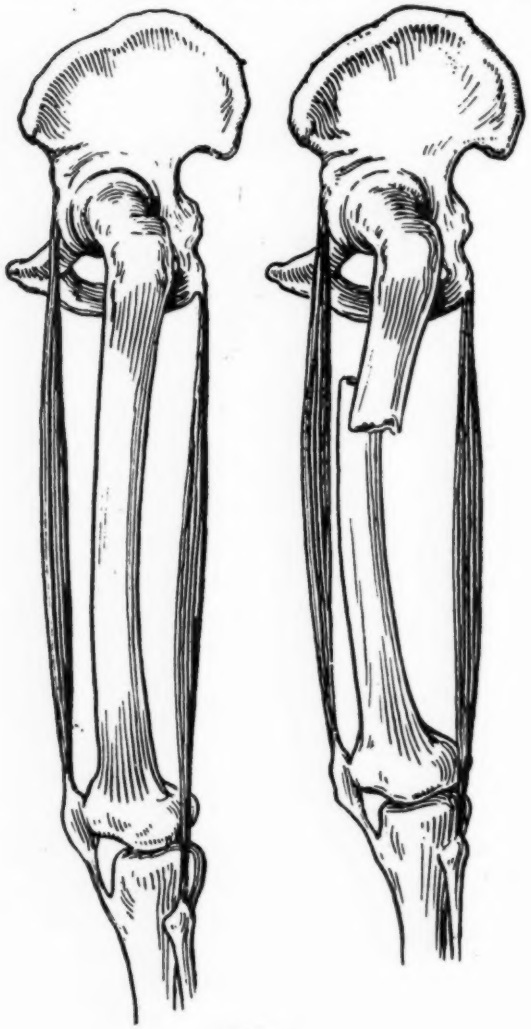

Fig. 1.

the relative position of the fragments in an anterior posterior view will be determined by the location of the fracture along this line; high the lower fragment will be displaced inward; low the upper fragment will be displaced inward. Two general forces are active at the time of fracture, one upward and one inward. Clinical histories of fractures of the femur show that most mechanical forces which have produced the fractures come from the ventral and lateral side of the patients and have forced the lower fragment backward and inward; subsequent contracture has kept the fragments in this relative position.

To overcome these muscle forces according to this method, the patient is placed in any ordinary hospital bed. A pillow is placed beneath the thigh and a smaller one below the calf of the leg. A sling is made by placing a large towel about the knee. Adhesive plaster is fixed to the leg in the usual way as in Buck's Extension. *The adhesive does not extend above the knee* (Fig. 3). A pulley is attached to the wooden rider (Fig. 3 D). A frame is secured to the bed so constructed that an overhead pulley (B) and two pulleys, one above the other and beyond the foot of the bed, may be utilized (C and E). One end of a stout cord of small diameter is attached to the towel sling and successively led through the pulley (B, C, D, and E). A weight is then attached to the free end of the cord and permitted to hang suspended from the lower pulley. The entire musculature of the thigh with the exception of inward or outward action of the adductors can then be placed in a state of balance. By applying the physical problem of the Parallelogram of Forces the direction and intensity of the pull can be estimated. The base line extends from the knee to the foot (A-D) and represents the downward pull of the Buck's extension, the other side is represented by the upward action of the towel sling (A-B). The diagonal (A-F) of a parallelogram erected with these two lines as sides is proportionate in degree, graphically showing the force and direction of the pull on the leg at the knee. It is evident that the direction and force can be controlled by the location of the overhead pulley and the amount of weight applied to the cord. The adductor factor is controlled by adduction or abduction of the leg. This necessitates for purposes of stability of the frame a lateral action at the extremities of the overhead bar, (Fig. 3). This is obtained by the use of a "T" and elbow connection between the uprights and the horizontal bar of the frame. Roentgen-ray examinations made at ten day intervals with the portable apparatus will guide the surgeon in determining the force and direction desired.

We have found it necessary to use about 12 lbs. weight. This is more than reported by either Dr. Russell or Dr. Ryan.[1] Children require very much less. In fractures high on the shaft, the pillow as well as the sling will by angulation assist in the reduction. In our experience with vigorous adults we have found that a rather firm pillow must be used beneath the thigh to overcome the tendency toward backward angulation at the site of fracture.

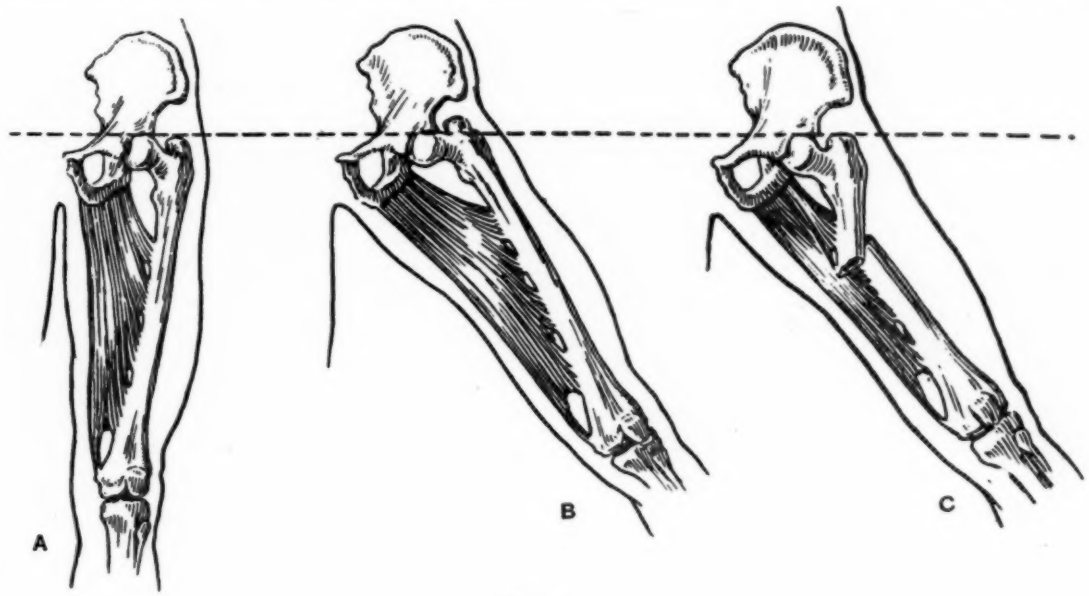

Fig. 2.

Roentgenogram 50684 (Fig. 4): Patient was an obese woman, seventy years of age. She had met with an automobile accident. Plaster spica had been applied. Roentgenogram after cast had been applied showed shortening. She complained so bitterly of the cast that the plaster was removed and the leg placed in Russell traction. The illustration shows the very generous amount of callous twelve weeks after the accident

Roentgenogram 56748 (Fig. 4): This illustrates well the reduction that was obtained in an epiphyseal separation of the lower end of the femur. The patient was admitted to the hospital wearing a plaster spica. Roentgenogram showed marked posterior displacement of the distal fragment. The cast was removed and the leg placed in Russell traction for four weeks. The roentgenogram shown here was taken at the end of that period. He was discharged able to walk without support, eight weeks after admission and nine weeks after the accident.

Roentgenogram 56220 (Fig. 4): This patient was a chauffeur, thirty-nine years of age.

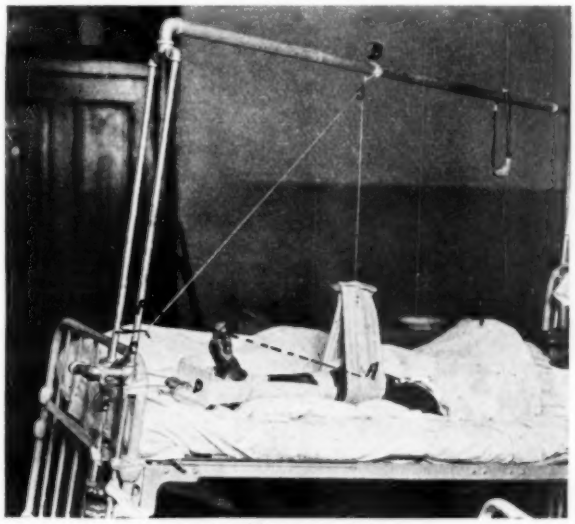

Fig. 3.

He had suffered a bilateral fracture of the mandible and a compound, comminuted fracture of the middle third of the left femur. He was placed in Russell traction. He developed a pulmonary embolus. The chest gradually cleared up. This roentgenogram of

[1] Ryan, T. J. *Ann. Surg.*, April, 1927.

the femur was taken one hundred and twenty days after the accident. He received calcium and cod liver oil while his fractured jaw was

average time in traction was forty-seven days with limits of thirty and ninety-two. Up to this time every case has demonstrated a very

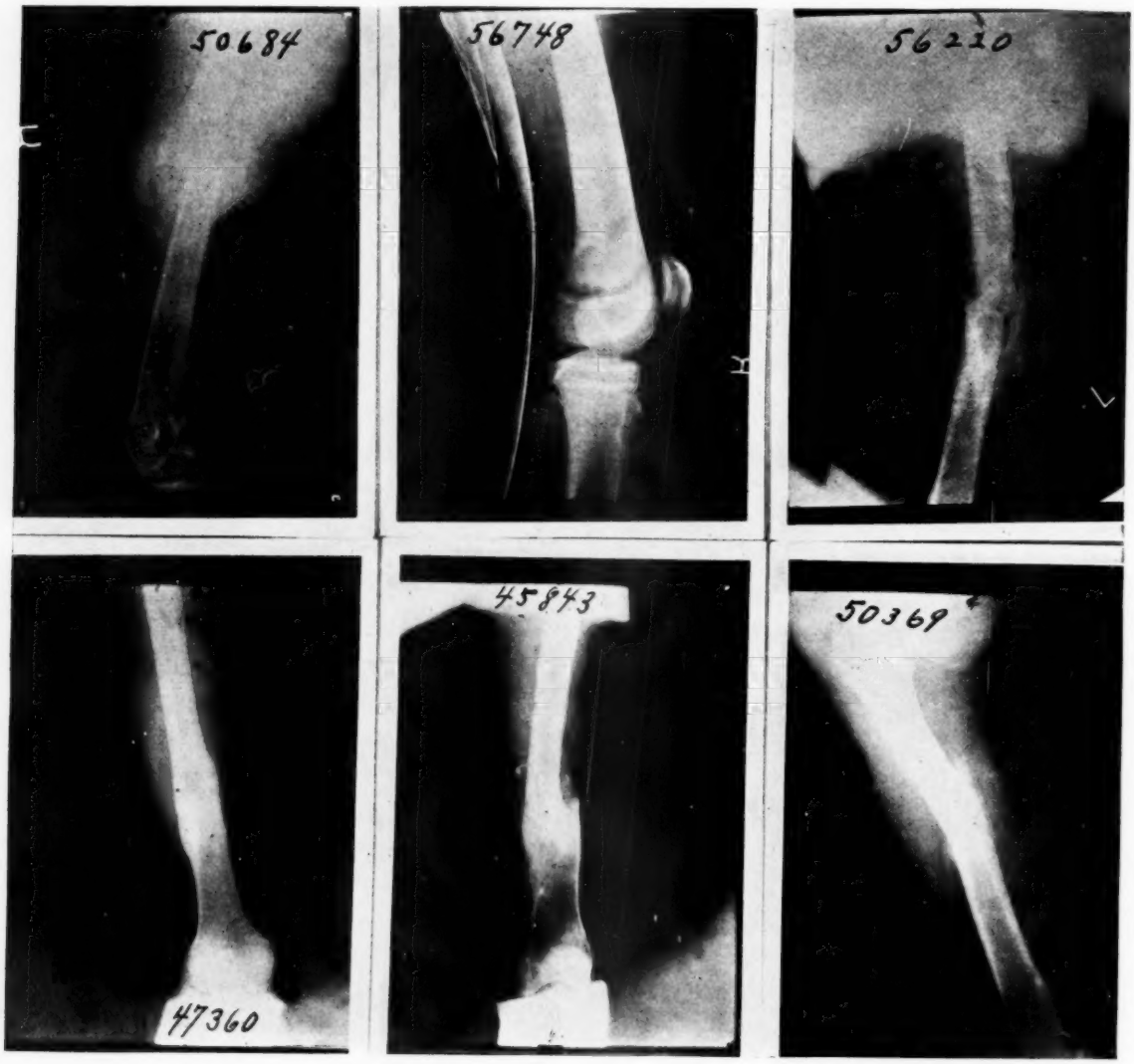

Fig. 4.

being treated. He did not make bone until he was able to take a regular diet. Knee joint at the time of discharge showed a motion of 120°. He has since returned to his regular occupation as truck driver.

Roentgenograms 47360, 45843, and 50369 (Fig. 4) show some end results. It will be noted that the alignment in these rather complicated cases was good. Shortening was practically negligible and a good functional result was obtained. The cases treated in this series were not selected because we felt they were ideal for this method but rather cases in which from the nature of the injury we expected difficulty in the use of previous methods. The active bone regeneration. The alignment irrespective of the character and location of the fracture has been unfailingly good. No limitation of motion of uninjured joints was noted.

As remarked by Russell, the details in the management of the cord, pulleys and frame, possess many possibilities in which house officer as well as patient have offered valuable suggestions. The attitude of the average patient has been one of very active cooperation. It is explainable chiefly because of the comfort that this method gives him. We have had the experience of

Case No.	Age	Sex	Occupation	X-Ray Finding	Days in Traction	Complications	Days in Hospital
45843	25	M	storekeeper	fracture middle and lower ⅓ of femur	49	none	59
46353	41	M	janitor	gun-shot wound fracture of middle and lower ⅓ of femur	42	foreign body compound fracture	52
46899	27	M	chauffeur	transverse fracture of middle and lower ⅓ of femur	52	fracture both femurs	139
47360	21	M	laborer	fracture middle ⅓ of femur	44	none	51
50369	36	M	structural steel worker	multiple fracture; spiral middle ⅓; spiral base of trochanter	45	Pott's fracture both legs, multiple, spiral fractures.	87
50684	70	F	none	transverse fracture middle ⅓ of right femur	56	senility	102
51530	7	M	school	fracture middle and lower ⅓ of femur	35	none	43
51630	1	M	none	fracture middle and lower ⅓ of femur	35	none	35
52659	6	M	school	fracture upper ⅓ of femur	35	none	41
53518	64	M	laborer	intra-capsular fracture neck of femur	70	none	84
56220	39	M	laborer	comminuted fracture middle and lower ⅓ of femur	92	fractured mandible	120
56748	17	M	school	epiphyseal separation of lower end of femur c long fracture into shaft	30	none	54
56873	35	M	livery man	transverse fracture below the trochanter	35	none	75
57813	5	M	school	fracture middle ⅓ of femur, oblique	56	scabies	72
58066	30	M	chauffeur	transverse fracture middle ⅓ of femur	48	none	60

seeing a patient who has had a particularly severe accident or suffered a long transportation go to sleep without narcotics before the details of the apparatus have been entirely completed. Nursing care is greatly lightened. Patients move and turn without pain. With rare exceptions they have been interested and helpful. Indeed this particular feature has induced us to occasionally remove the plaster from a complaining patient who has had an intracapsular fracture and at this time we feel that with the aid of some method of inducing internal rotation this method may well be used in such cases.

Dr. Russell states that after proper alignment has been secured it is not necessary to apply plaster to maintain approximation of fragments. "The purpose of operation must only be to enable fragments to be brought into position; and operation is not justified when its purpose is merely to keep them there." Should there be interposition of soft parts which is shown by a persistent shortening he opens the thigh, cuts across the interposing tissue, closes the wound and then treats the case in the usual manner. We have not found it necessary to do an open operation.

CONCLUSIONS

The results we have experienced in the treatment of fractures of the femur by the Hamilton Russell method of traction have shown:

1. No case of non-union
2. No open operation
3. General alignment in all cases satisfactory
4. No joint changes
5. Period of treatment shorter than by any other method in our experience
6. Patients unusually comfortable and cooperative.

MECHANICS IN WEAK & FLAT FEET*

GEORGE ANOPOL, M.D., F.A.C.S.

NEW YORK

ANY topic referring to diagnosis and treatment of foot conditions attracts a great deal of attention. And yet weak and flat feet are very often overlooked not only by the general practitioner but by many specializing in orthopedic surgery.

The symptomatology is variable: in one case it is tiredness in the muscle of the leg, in another pain in the arch region, while still others may complain of pain about the knee, thigh, hip or back. All these are due to disproportion of muscle pull.

The mechanics of the foot should be clearly understood by those attempting to make a definite diagnosis of weak and flat foot. Once understood, the patient in the majority of cases can be relieved however, there is probably more medical shopping by patients with foot conditions than with any other orthopedic condition. Arch trouble is muscle trouble and until this is realized many conditions will go unrelieved. The bony frame work is of course necessary. It is by means of this that proper directions and relationships of the muscle pull are kept.

The longitudinal arch is one of prime importance when considering the weak or flat foot. Metatarsalgia if unrelieved will in time produce a secondary weak or flat foot. Other conditions such as hallux valgus, exostoses, spurs, os calcis, etc. all play a rôle in producing cases of weak and flat feet.

Focal infections such as are found in the teeth, throat, sinuses and colonic tract also play an important part as predisposing causative factors of weak and flat feet. The colon particularly should not be overlooked, because very often, long after the foci in the head have been removed, the toxic condition in the colon continues. The absorption of these toxic substances weakens the muscle power, or through its irritation produces a fascitis which unbalances the muscle pull. Patients presenting these latter conditions will not be relieved by the method to be described unless the toxic condition is taken care of properly at the same time. More and more of these cases are seen to be complicated by intestinal (colonic) toxemias.

The bones making up the longitudinal arch from posterior to anterior are, as you will recall, calcaneum, cuboid, and metatarsal. The calcaneum points upward obliquely anteriorly. It rotates about its own axis when the calf muscles contract or relax if the opposing group of muscles is not working in proper mechanical coordination. This is very important to remember.

The anterior tip of the os calcis makes up part of the apex of the longitudinal arch.

The foot is a two-arm lever machine, one long and the other short. The short arm is that from the insertion of the tendon achilles on the os calcaneum to the center of the ankle joint. The other is from this point to the metatarsal phalangeal joint. The ratio is approximately 1:2, i.e. if 10 lb. pressure is exerted on the ball of the foot, there is 20 lb. pull exerted on the calf muscles, or twice the amount. A patient weighing 150 lb. therefore exerts 300 lbs. pull on the calf muscles every time he takes a step.

This knowledge is of assistance to us when examining patients for the conditions under consideration. Irrespective of where the symptomatology may be, if the patient complains of strain in the calf muscles, especially at the origin of the gastrocnemius muscle, when the foot is dorsiflexed with the knee extended, that patient should be taken care of from the weak foot standpoint and, if the arch is markedly depressed

* Submitted for publication March 16, 1929.

when standing, from a flat foot standpoint. Many weak feet have arches that appear within normal limits as to height. And many are too high.

When the patient is questioned carefully, in early cases of weak feet tiredness in the leg muscles is complained of; in more pronounced cases it is ache.

The more important muscles whose line of pull must be considered are the gastrocnemius and the tibialis anticus. In mechanics it is a law that less power is necessary to pull in a straight line than when the line of pull is changed. The gastrocnemius is a powerful muscle pulling in a straight line; the pull of the anterior tibialis is changed due to its attachments. Disproportion in the pull of the two sets distorts the longitudinal arch. The more contractions of the calf muscles, the flatter becomes the arch-the calcaneum rotates about its axis. This produces a more acute angle over which the anterior tibialis has to pull. A vicious cycle is thus produced. The anterior tibialis becomes overstretched. Nature then takes up the slack in the gastrocnemius group. High heels and post traumatic conditions of the foot and leg when put up in the equinus position, produce a similar condition. On examination the foot cannot be made to dorsiflex to a right angle when the knee is extended.

As to treatment, the underlying foci for toxic absorption should be carefully considered and eradicated, while the condition is being treated locally.

The old recommended exercise of tiptoeing do not aid in correcting these foot conditions. They overdevelop the group of muscles that from a mechanical standpoint should be weakened to allow the anterior end of the calcaneum to come up when the tibialis anticus muscle contracts.

Exercises that tend to develop the tibialis anticus and stretch the gastrocnemius group are the ones to be recommended. These are toeing forward, raising the arches and charging, both heels being kept on the floor. This corresponds to dorsiflexion of the foot, which act pulls down on the insertion of the gastrocnemius; and the extension of the knee pulling the origin upward, thus stretches the muscle. With a relaxed gastrocnemius group, it permits the tibialis anticus to pull up the arch and reestablish the normal relationship of the muscle pull.

In early cases proper foot gear and these exercises supplemented by toeing in when walking and keeping the arches actively elevated when standing at all times, soon relieve the patient of his or her weak feet. However, once weak feet, always weak feet. It means constant care.

The more aggravated cases are strapped with adhesive tape at intervals of six or seven days. At the same time the patient is fitted with proper type shoes in the particular case; a high lace shoe should be used, irrespective of ideas in fashion. These strappings are repeated until the condition improves, i.e. the patient is more or less free from symptoms and on examination the usual strain in the calf muscles is absent when the foot is dorsiflexed to beyond a right angle, with the knee extended. At this time an impression of the arch or arches is made with plaster of paris from which the brace maker constructs the Whitman Flange Plate. This must be carefully adjusted by the surgeon at the time of delivery and at intervals of several weeks at first and later months.

The strapping should be done properly. However each one believes his method is the method. It is not so. The dressing should be of a supporting nature and prevent edema of the toes and foot.

The adhesive tape used is 1½ to 1¾ inches wide. Two strips about 14 inches long are applied as follows: The first is started on the outer aspect of the tarsus, the posterior edge of the adhesive tape is placed just anterior to the external malleolus. The second strip is superimposed over the first except that it is placed about ¼ to ⅜ inches farther anteriorly. While these are applied the foot is well dorsiflexed, and the knee also flexed to relax the gastrocnemius group.

These strips pull the anterior portions of the calcaneum and thus the apex of the arch. This procedure stretches the gastrocnemius group tendon and relaxes the anterior tibialis. Nature will take up the slack in the tibialis anticus muscle.

These two strips are held in place with circular strips overlapping each succeeding one. This is important for the comfort of the patient, for ridges of skin between two strips of adhesive tape make for a very uncomfortable condition. The circular strips are started on the dorsum of the foot and put on from medial to planter, to lateral and back to the dorsal surface. When put on in this way a comfortable dressing is applied quickly. The edge at the base of the toes is slit between the third and fourth digits, never laterally over the fifth metatarsal. Another slit is made just posterior to the medial malleolus, and never over the achilles tendon insertion.

After this type of supporting dressing, when the patient is symptom free, the impressions are made. The patient is seated comfortably on a chair so that the thighs are at a right angle to the leg and the leg at a right angle to the foot. The foot points forward. There is no weight bearing upon the plaster.

If impressions are made before the patient is relieved of symptoms, a support will be made that will not support. The type plate made is the Whitman Flange. The plate holds the foot in position, preventing overstretching of the already weakened tibialis anticus muscle. It also reflexly irritates the arch region and the patient rather than stand on the plate walks on the outer edge of the foot, thus developing the tibial muscle.

There are those who object to the rigid foot plate because it interferes with muscle development. This is erroneous in that contractions of the muscles of the leg and foot raise the arch from the plate. The planter fascia is usually overstretched when the patient comes for treatment and thus it need not be considered in the use of the rigid plate.

COLOFIXATION IN "CHRONIC APPENDICITIS"*

BASED ON A STUDY OF LATE RESULTS IN 96 PATIENTS

E. P. QUAIN, M.D., F.A.C.S.

BISMARCK, N. D.

IF we should become sticklers for nomenclature and refuse to give the ending "itis" to any pathological specimen which does not show microscopical evidence of inflammation, the number of cases of chronic appendicitis would be found to be relatively few. Appendices removed after an acute attack has entirely subsided often show a surprising absence of macroscopic evidence of previous infection. Microscopically, there may be found an increase of fibrous tissue and a suggestion of edema at the place of a healed mural abscess or a few bands of adhesions indicating where the infection had gone through the appendiceal wall. Most of the appendices removed for so-called chronic appendicitis are so similar to normal appendices removed during laparotomies for other lesions that the pathologist rarely can tell them apart.

This, of course, should not be understood as a criticism of the removal of appendices which by reason of their malposition cause symptoms, ablation of the appendix after acute attacks, nor the routine appendectomy while the abdomen is opened for other reasons.

The difficulty in recognizing the various forms of visceroptosis comes from the fact that the symptoms produced resemble very closely those of some other organic lesion with which we are already more or less familiar. Thus, for example, a simple gastroptosis or a duodenum obstructed by a dragging mesentery may produce pain and distress almost identical with duodenal ulcer, and nephroptosis may often suggest gall-stone colic.

The most common source of error in making a diagnosis of chronic appendicitis is the fact that ptosis of part or all of the right colon often produces a train of subjective symptoms which simulate very closely those we formerly ascribed to chronic inflammation of the appendix. It is my belief that this statement has been definitely proved by the clinical material reported herewith, and from the following general observations:

1. We have seen a number of patients with the classic symptoms of chronic appendicitis who at operation were found to have hypermobile right colon with pericolic membranes and were not relieved of their right-sided pains after appendectomy.

2. When the same patients were reoperated on and colofixation made, their symptoms disappeared.

3. If colofixation alone is made in this type of patients, and the appendix is left in situ, the symptoms of "chronic appendicitis" disappear exactly as in those from whom the appendix was removed at the time of operation.

Right colofixation has been performed by myself and my associates in over 300 patients. However, in fully half of the number some other intra-abdominal technique, in addition to appendectomy, was followed out and it is often difficult to decide what part of the postoperative relief should be accredited to each procedure. The cases chosen for this report, therefore, are only those in which no other intra-abdominal operation than appendectomy and colofixation, or colofixation alone, was performed which might influence the subsequent symptomatology.

The report is based on information

* Read before Western Surgical Association, Chicago, Dec. 15, 1928.

gained through interviews, re-examinations and letters from 96 postoperative patients from one to seven years after operation. the average time being three and one-half years. Fourteen of the patients were males and 82 females. Their ages ran from ten to forty-five years, the average being twenty-four. With the exception of a few who were operated on near the onset of symptoms, under the diagnosis of acute appendicitis, the duration of the trouble had been chronic in nature. Several had had right-sided pain for ten or fifteen years.

The most prominent and in many instances the only symptom of which the patients complained was pain in the lower right abdominal quadrant. The pain was described by 66 patients as constant in nature. About half of this number had noted an increase of the distress after standing on their feet a long time, after hard work, and when constipation was aggravated. Some had learned to find temporary relief in the recumbent posture, and especially when lying on the right side. The pain had rarely been severe enough to cause the patient to go to bed.

Three of these patients complained of mid-abdominal pains after meals as even more distressing than the right-sided pain. These were entirely relieved after colofixation. Constipation was present in about half of this class of patients.

Another type of symptoms was represented by 27 patients who had had definite *attacks* of pain in the right abdomen. The attacks varied in number from 2 or 3 to 15 or 20, depending on the number of years' duration of the illness. The severity also varied from a sensation of "gas" and moderate discomfort in some cases, to sharp and definitely localized pains in others, compelling the patient to go to bed for a few hours, or for a day or two. Physicians had been consulted by several of these patients during the attacks and invariably the diagnosis of appendicitis had been made and operation advised. Sixteen of the 27 had vomited during the attack, and several others had distinct nausea, but did not vomit. The emesis in each case had taken place not at the onset of the pain, but usually several hours later.

Continuous pain near McBurney's point was the outstanding symptom during the attack in all these patients. The point of greatest tenderness, however, was usually a little higher and farther out on the flank than is the case in acute appendicitis. With this disease in mind the local tenderness was also found to be much less marked than one would expect from the history of pain and disability. One or at most two degrees' elevation of temperature was present in about half of the cases seen in an attack. The leucocyte count, as a rule, remained normal. A day or two in bed or at complete rest from the patient's usual work marked the end of each attack.

It is my duty to confess that some of these patients were operated on during the painful attack under a suspicion that an acutely though mildly inflamed appendix was the cause of the symptoms. But in these cases the appendix failed to show the usual signs of acute inflammation. It was of normal or subnormal dimensions and in proper relation to the cecum. The only abnormal condition which could warrant any belief that painful symptoms ever had been produced by the appendix was in some instances when it was found involved in pericecal membranes.

However, there were two definite abnormal findings in these patients' abdomens. First, there was hypermobility of the cecum and part or all of the ascending colon, and second, a pericolic membrane attaching the colon loosely to the lateral abdominal wall. When operation was made during the attack, the pericolic membrane appeared more intensely reddened from the acutely injected blood vessels than when operation was undertaken a few days after the attack. By taking hold of the colon and pulling it into the wound, it was noted that the pericolic membrane tautened before the pull became evident on the mesocolon.

Microscopic examinations of the appendices removed both during and after the attacks have not shown any deviation from

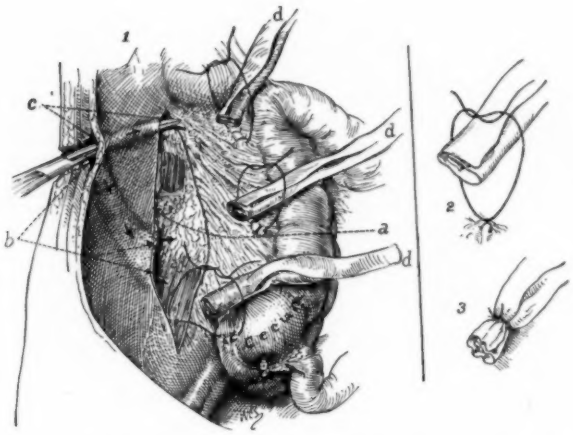

Fig. 1. Showing incision in posterior peritoneum and placing of cigarettes. If entire right colon requires fixation, cigarettes (d) are passed through two separate tunnels (b,c) but through same stab wound in skin and muscles. Peritoneal margin (a) is raised with finger while cigarettes are pulled into place.

normal. There was an absence of the acute congestion and the infiltration of the submucosa seen in acute appendicitis, even when the attack is very mild, or subsiding. The appearance of the pericolic membrane as described by our pathologist, Dr. L. W. Larson, is that of " . . . a thin, hyperemic smooth-surfaced membrane. Microscopically, these membranes are found to consist of a loose areolar and fibrous tissue which usually is very vascular. No evidence of an inflammatory reaction has ever been noted in the numerous specimens submitted for examination."

In our first experiences with colofixation, when the colon was sutured into an incised wound in the posterior peritoneum and the abdomen closed without drainage, we saw an occasional infection following the operation. The infection was never alarming in nature, but sufficient to demand some revision in technique. Its focus seemed to be not at the appendiceal stump but outside the ascending colon. It seemed probable that the incision into the retroperitoneal tissues might have severed some aberrant lymph vessel containing colonic bacteria. Patients with marked coloptosis and chronic cecal stasis usually have a definite adenopathy behind the ascending

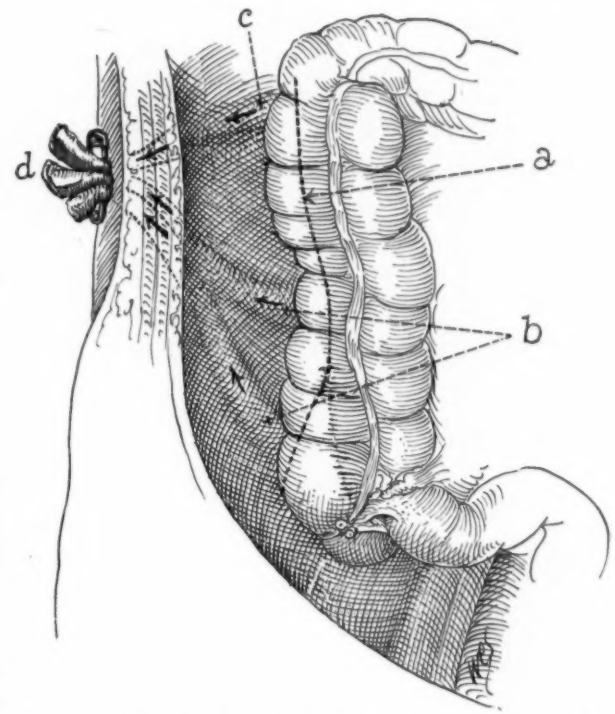

Fig. 2. Colon resting in its new retroperitoneal bed. Dotted line indicates approximate extent to which external peritoneal margin will reach.

colon. The pus obtained from the cases mentioned always contained coli bacilli.

A few of our earliest patients returned after a few months, stating that the side aches had reappeared, especially when standing on the feet for a long time, or after heavy work. The operative record from these cases showed that only a small opening had been made in the posterior peritoneum into which the mobile cecum had been affixed with 1 or 2, or at most 3, sutures. The constant pull on a small area of adhesions had developed a new ligament from which the colon was again suspended, causing pain. Such patients were permanently relieved of pain after a second operation when the area of fixation was extended over a surface approaching more nearly the normal.

The radical fixation of the colon by means of sutures requires an incision, or incisions,

of liberal size. The time occupied in the necessarily complete hemostasis and in the placing of the fixation ties may be longer

Fig. 3. Photograph showing marked cecum mobile lifted out through wound, with forceps passed under pericolic membrane.

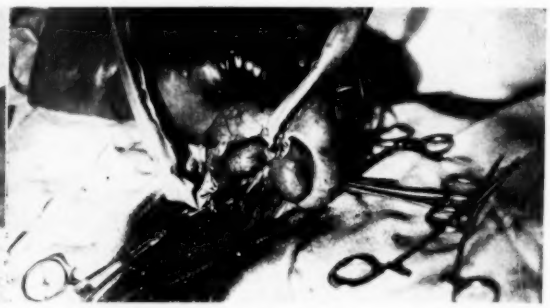

Fig. 4. Same case. Appendix removed and cecum sutured deeply on stump of mesoappendix. Two cigarettes fastened near external logitudinal line of ascending colon.

than desirable. The deep retraction needed may become unduly traumatizing.

In order to overcome all these objections a simpler, though perhaps less elegant, technique was adopted about three years ago. This method consists in making an opening through the posterior peritoneum from the psoas major muscle upward to a point near the lower pole of the kidney, partly with scissors, and partly by blunt separation of the tissues. Two or three catgut sutures are placed through the serosa at or near the posterior longitudinal line of the colon. The end of a small rubber cigarette drain is tied to the colonic margin with each catgut. A short incision is made in the flank and the cigarettes are withdrawn with a long blunt forceps and anchored with a safety pin outside the stab wound. The external peritoneal margin is lifted up and allowed to fall loosely against the colon as the cigarettes are drawn into place.

It is important to study the anatomic relations, extent of mobility and possible abnormal locations of neighboring organs before the fixation is made. The cecum and ascending colon should be made to rest easily in their newly prepared retroperitoneal bed, without tension on blood vessels, mesenteries, or peritoneum. It seems plausible that when the fixation is made with a series of sutures the attachment may be too unyielding at some segment or other, producing a temporary restraint

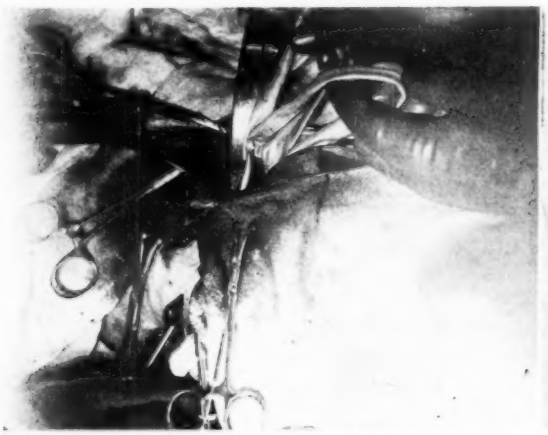

Fig. 5. Same case. Long forceps passed bluntly through stab wound in skin above crest of ilium and cigarettes grasped and ready to be pulled into wound made in posterior peritoneum.

Fig. 6. Same case. Cigarettes are pulled into place and anchored in stab wound with safety pin. Fingers holding cecum to determine proper degree of tension.

to the peristaltic wave and causing an unnecessary distress immediately after the operation. Since we began to make longer and wider separation of the posterior peritoneum and the subperitoneal fat and to implant the colon more loosely over a larger area, the patients have had a much easier immediate recovery after operation, and the later results have been all that could be expected.

The rubber cigarettes serve as a temporary anchorage, until sufficiently firm adhesions have formed to hold the colon permanently in place. They are fastened rather loosely, permitting some motion and readjustment of the posterior colonic wall to accommodate the peristaltic movements. They also act as a mild irritant to hasten the formation of adhesions and give the additional advantage of immediate drainage of the lymph and blood which always ooze into the dissected area. Ligation of retroperitoneal blood vessels is rarely required when the cigarette is used. This is time-saving and the omission of sutures to the peritoneal margin further simplifies the procedure. The total time for the entire operation should not be over four or five minutes beyond that required by a given operator for an uncomplicated appendectomy.

In some instances we have made use of long strands of catgut fastened to the colon in this transparietal method of fixation. Long pericolic membranes and fascial strips taken from the external oblique muscle have also been used for the same purpose, but none of these methods have all the advantages of the rubber cigarette.

Most of the patients experience considerable "gas pain" the first two days after colofixation, but enemas and pituitrin are usually successful before the third day is over. Some have a surprising absence of distress in spite of the extensive trauma.

The cigarette loosens and comes out in six to nine days and the patients leave the hospital three or four days later. It is our practice to advise them on leaving the hospital to avoid all strenuous work and to rest in the recumbent posture several hours a day during the next two weeks or more. Female patients with relaxed abdominal walls are fitted with an abdominal binder to be worn a few months after operation. However, we have repeatedly seen energetic young patients disregard all this advice and apparently without any harm. It has appeared from postoperative roentgen-ray studies of the colon that in about two weeks the cecum becomes sufficiently adherent in its new bed to withstand permanently the forces of gravity.

Fig. 7. Same case. Wound closed. Forceps on anterior superior spine to indicate position of split muscle incision.

Of the 96 patients 84 were entirely relieved of their former abdominal pain and distress; 9 stated that they had occasional pains in the right abdomen and 3 said there had been no improvement. Investigation indicated that there was a somewhat higher percentage of remaining pains in the cases where sutures were used exclusively than in those where the fixation had been made with rubber cigarettes and with few or no sutures. There was no mortality in this series. Constipation was cured in about two-thirds of the number in whom this defect was a prominent feature. Of the 32 so afflicted 20 had used no laxatives after the operation, while several of the remaining needed less than formerely; 5 had noted no improvement.

Chronic constipation is a common complaint among coloptotic patients. Why a

freely movable colon should encounter more difficulty in carrying on its propulsive peristalsis than a colon attached to the unyielding abdominal wall over one-third of its circumference is not easy to understand. Occasionally, hypermobile colons are seen with a musculature of even greater thickness than normal, and yet the patients may be chronically constipated and addicted to daily laxatives. One must conclude that the evident hypertrophy is due either to a defective nerve supply which produces too close a balance between peristalsis and the physiological antiperistalsis in the right colon, or that the contraction waves of peristalsis are ineffective because of the absence of fixed and stationary starting points. The latter is the opinion of Barclay who describes the mechanics of the peristaltic wave as requiring a fixed point upon which its successful movement must be based. My experience tends to confirm this view.

A gain of weight reported by 52 patients may be partly explained by the fact that many of them were young and would in the natural and healthy course of events experience further development. But there must be another reason for a very marked increase in weight in a number who were over twenty-five years of age. The average gain in 14 patients between the ages of twenty-two and forty, who were able to give exact information, was 19½ lbs. Several of those who were thin, anemic, sallow, "neurotic," under-weight and of the typically visceroptotic appearance before operation had gained 20 to 30 pounds in weight in a few weeks after colofixation.

Three patients who, in addition to the characteristic local pain, had suffered from periodic attacks of painless and evidently non-infectious diarrhea for several years without known cause had no further bowel disturbance after operation.

In complete right coloptosis the weight of the cecum and ascending colon and their contents is exerted from the region of the solar plexus above the duodenum. In such patients epigastric symptoms are often found which can be determined radiographically to be caused by the obstructed duodenum. Symptoms in the lower abdomen due to the abnormal colon may or may not be present in such cases. But in either case it would be a surgical error to treat the duodenal lesion before lifting and fixing the colon in such a manner as to remove the stenosing drag on the duodenum. We have seen a number of patients of this type, with nausea, bile emesis, headaches, and distress after eating, who have been entirely relieved without duodenojejunostomy, after a radically executed right colofixation. The patients in this series who were relieved from distress after meals undoubtedly belong to this class.

Another feature noted among some of these patients was a relief from a certain form of nervous symptoms for which we often cannot find any better name than "neurasthenia." Some of them had been treated as pure neurotics by their previous medical attendants.

In 14 of the 96 the appendix had been removed at some previous operation; 11 of these considered themselves cured and 3 were definitely relieved from pain after colofixation. Although in some of these one might suspect that the release of some postoperative adhesion about the cecum had a bearing on the improvement, the complete relief from pain in several who had no adhesions and where nothing whatever was done in the abdomen except colofixation presents no other reason for the cure than the colofixation.

Colofixation was made in 4 patients from whom the appendix was not removed. One was a hardworking woman, forty years of age, a multipara, who had had a constant pain in the right abdomen for over a year. She was chronically constipated and used laxatives freely. Appendicitis had been diagnosed and the conventional treatment advocated. According to our conviction, she suffered from right coloptosis; and she was treated with a corset and pad for a time. This improved the condition, but not

sufficiently to make her entirely comfortable, and operation was performed. The cecum and ascending colon were found hypermobile and suspended from a narrow membrane attached above the anterior superior spine of the ilium. The appendix was very short, but otherwise of normal appearance and relations. Radical colofixation was made, but the appendix, for the purpose of a "test case," was left entirely undisturbed.

This operation was performed in May, 1921. This woman was immediately relieved of her pains and has enjoyed good health ever since. Moreover, she has had no need for laxatives since the operation.

Since that time we have made 3 similar "test cases." Two were in young women who had constant pains and aches in the right abdomen, and the third was in a man of twenty-six who had symptoms suggesting "recurrent appendicitis." The appendices in all these were either small or of the obliterating type. Their symptoms disappeared in all 3 after colofixation, as in the first case.

There can be no mistaking the source of the painful symptoms, nor the cause for the relief in these 4 patients. They were intelligent individuals and busy in their occupations, but more or less handicapped from pain. Since operation they have been well, from two to seven years respectively, and express their complete satisfaction with the outcome.

It cannot be denied that since the appendix was removed in the majority of these cases, its removal may have had a distinct influence on the freedom from symptoms in a certain number of the patients. Some of the appendices were found in abnormal locations and some had evidence of former inflammatory conditions. But the total number of such appendices was comparatively small. The great majority were normal, macro- and microscopically, while some were of the obliterating type.

The local pain and discomfort produced by the hypermobile cecum and ascending colon, especially when these organs cause a pull on the abdominal wall by means of pericolic membranes, are the same symptoms we formerly considered diagnostic of chronic appendicitis. The purpose of the present contribution and case report is to emphasize this fact and to encourage a wider recognition and study of this common pathogenic condition.

SUMMARY OF CASE REPORTS

Patients "followed up"	96
Years since operation	1 to 7
Males	14
Females	82
Ages, 10 to 45 years; average	24
Duration of symptoms, average years	2½
Pains constant and chronic	66
"Attacks" of pain	27
Constipation severe	32
Emesis during attack	16
Nausea without emesis	5
Pain after meals	3
Diarrhea during attack	3

RESULTS FROM ONE TO SEVEN YEARS AFTER COLOFIXATION

Complete relief from pain	84 (87.5 per cent)
Improved	9 (9.3 per cent)
No improvement	3 (3.2 per cent)
Constipation cured (in 32 cases)	20 (62.5 per cent)
Constipation improved	7 (21.9 per cent)
Constipation not improved	2 (15.6 per cent)
Constipation worse	3

APPENDECTOMY FOR ACUTE PERFORATED APPENDICITIS WITH SPECIAL REFERENCE TO THE PREVENTION OF WOUND INFECTION*

FRASER B. GURD, M.D., F.A.C.S.

MONTREAL, CANADA

WHEN the surgeon is called upon to see an individual suffering from cute appendicitis, three problems present themselves. In the first place and the necessity for instituting operative procedures at such a time, and in such a manner, that if possible the life of the patient may be saved is paramount. Although in the majority of cases no serious anxiety on the part of the surgeon exists regarding the probable outcome as regards life, there are, nevertheless, still a certain percentage of cases which, as the result of either too late diagnosis or the exhibition of a purgative, or both, are not seen until it is evident to even the casual observer that the patient's life is in jeopardy.

The likelihood of a fatal termination of the disease not presenting itself, two other most important problems require consideration. In the first place, the period of invalidism and disability should be shortened to a minimum, and, secondly, the patient should be discharged with a sound abdominal wall, and free, in so far as possible, from intraabdominal adhesions which might be considered to constitute a possible cause of future digestive disturbance or of actual obstruction to the passage of contents through the bowel tract.

The author is of the opinion that since the use of a definite technique in the operative treatment of acute suppurative or gangrenous appendicitis, the employment of which was commenced in 1917, not only has there been a lessening of the mortality rate in that certain types of cases that previously resulted in a moderately high percentage of deaths now run a comparatively uneventful postoperative course, but, in addition, the incidence of postoperative abdominal wall weakness or herniae has been almost eliminated. More particularly, however, the period of disability and invalidism has been markedly shortened.

The patient's postoperative discomfort has been lessened to an important degree and the number of dressings cut to a fraction of their former number.

All surgeons will, I believe, agree that next to a progression of the disease to a fatal termination the most disturbing feature in the treatment of acute appendicitis with gangrene or peritonitis, or both, has been the occurrence in a comparatively large proportion of cases of a diffuse suppurative cellulitis of the abdominal wall, associated, as it is in many cases, with necrosis of the aponeurotic layers. When the technique described in this contribution is employed such a complication is almost completely avoided.

It is not my intention in this communication to dwell at any length upon the subject of faecal fistula. There is, I believe, a unanimous opinion, with which I most heartily agree, that rubber tube drainage is primarily responsible for this extremely annoying complication. Since the adoption of the technique recommended in this paper many hundreds of cases have been treated by the author and his associates without the development of a single faecal fistula.

In 1919[1] the author, in an article in which an attempt was made to indicate the useful adaptations of Rutherford Mor-

[1] Gurd, F. B. *Canad. M. A. J.*, 9: 625, 1919.

* Submitted for publication January 17, 1929.

rison's technique to civil surgery, described a definite technique. The specific purpose of this procedure was the prevention of contamination and consequent infection of the abdominal wall during operation for removal of the appendix in perforated and gangrenous cases.

The essential features of the technique recommended were as follows: The wound of the abdominal wall is accomplished down to, but without incising, the peritoneum. It is immaterial which of the usual incisions, which may be employed for removal of the appendix when this organ is acutely inflamed, is chosen by the surgeon. Since 1913 the author has made use of the laparotomy incision with which the name of G. G. Davis is associated.

The wound through skin, subcutaneous tissue and aponeurosis having been made, and the muscle having been drawn aside, careful haemostasis is carried out, at the same time avoiding, in so far as possible, the employment of ligatures. The whole wound is then thoroughly drenched with alcohol in order that the superficial tissues may be dehydrated. The alcohol is dried off, within one minute of the time of its application, and all exposed tissues carefully rubbed with B.I.I.P.[1] Excessive B.I.I.P. is removed by means of a dry gauze swab. Then, and only then, the peritoneum is opened.

As a result of the technique described above, all parts of the abdominal wound are coated with a thin waterproof layer of the paste; in consequence it is believed that contamination of the tissues themselves does not, and cannot, take place. If upon opening the peritoneum purulent fluid is encountered, or a gangrenous appendix heavily infected with both aerobic and anaerobic bacteria is drawn out through the wound, the protective covering of B.I.I.P. prevents contamination of the abdominal wall.

In the latter part of 1924, when the author assumed charge of the surgical service at the Western Division of the Montreal General Hospital, he introduced the technique already described by him in 1919, and again in this article, on the treatment of acute appendicitis. During the three years, 1925–1927, the method was employed on the author's service, but not by the other surgeons making use of this hospital. An analysis of the cases of acute appendicitis for these three years shows that approximately the same number of cases were treated in each of the two groups. Of 358 cases, 198 were treated on my service and 166 by the other group.

TABLE I

CASES OF ACUTE APPENDICITIS TREATED ON AUTHOR'S SERVICES

Total No. of Cases	Non-Perf.	Deaths	Days in Hosp.	Perforated	Deaths	Percentage Mort. Perforated Cases	Days in Hosp.
192	125	0	11.92	67	3	4.48	16.78 (excluding fatal cases)

TABLE II

CASES OF ACUTE APPENDICITIS IN SECOND GROUP

Total No. of Cases	Non-Perf.	Deaths	Days in Hosp.	Perforated	Deaths	Percentage Mort. Perforated Cases	Days in Hosp.
166	125	0	13.86	41	7	17.07	27.73 (excluding fatal cases)

Tables I and II show that although the acute non-perforated cases of the author's service remained in hospital approximately the same length of time as those in the other group, the perforated cases in the second group required hospitalization for eleven days longer than those treated by the author's technique. In other words, the

[1] Bismuth, Iodoform, Paraffin Paste containing bismuth subnitrate 2 parts, powdered iodoform 1 part and liquid paraffin about 1 part, or sufficient to make a thick paste. It is of the utmost importance that vaseline or paraffinum molle be not used, as with such a vehicle an ointment which will not adhere to the raw tissue surfaces results.

cases treated by other methods remained in hospital a 65 per cent longer period of time.

Although the total number of cases is not large, and the number of deaths in both groups gratifyingly small, the fact that the percentage of deaths among the perforated cases was only 4.48 per cent among the author's cases as compared with 17.07 per cent among the second group would appear to prove that the technique recommended is at least harmless.

In 1921 Eberts and McKim[1] published the results of an analysis of all the cases of acute appendicitis operated upon on Dr. Eberts' Service of the Montreal General Hospital for a period of two years ending June 30, 1920. This analysis indicates, I believe, the type of case presenting itself in our Montreal hospitals and the results of treatment by the methods previously employed. *Inter alia*, this analysis showed the following facts to be true:

Table III

	Non-perforated	Perforated
Average number of days in hospital	13	33
Mortality	0	16.9 per cent

This table did not include 4 cases of fecal fistula, each of which were in hospital over one hundred days.

In April, 1927, McKim[2] published an analysis of the cases of acute appendicitis operated upon in the same service for the years 1923–1925.

Table IV is taken from McKim's paper.

As McKim points out, certain differences are apparent on comparing the results during the years 1923–1925 with those reported for 1919–1920. These differences consist in: (1) Reduction of the average number of days in hospital for perforated cases from thirty-three to twenty-five:

[1] Eberts, E. M., and McKim, L. H. *Canad. M. A. J.* 11: 443, 1921.

[2] McKim, L. H. *Canad. M. A. J.*, 17: 434, 1927.

Table IV

Year	Cases	Perforated			Mortality Percentage			Days in Hosp.	
		No.	Percentage	Died	Perforated	Non-perforated	Total	Perforated	Non-perforated
1923	68	27	39.9	1	3.7	0	1.4	26.5	12.2
1924	81	29	35.7	4	13.8	0	4.9	27.1	13.4
1925	70	31	44.2	2	6.4	0	2.8	22.1	14.7
	219	87	38.9	7	8.2	0	3.1	25.1	13.5
1919–20	..	..	44.0	..	16.9	0	...	33	13

(2) Reduction in mortality rate in the same group from 16.9 to 8.2 per cent.

Whereas in the first series cases of fecal fistula were excluded in determining the average number of days, all cases were included in the second series except those patients who died immediately following admission.

In his contribution McKim expresses the opinion that both the change in mortality rate, and more particularly the reduction of the number of days in hospital, were due to the adaption on Dr. Eberts' service, to which the author is attached, of the author's technique. This technique, which was first described in 1919, was gradually adopted by more and more of the surgeons on the service until by the year 1923 it was being employed as a routine procedure in every case suspected of perforation.

The author is familiar with the fact that, in certain clinics, strong objections are still maintained to the employment of B.I.I.P. on the grounds that it is dangerous. It is unfortunately true that in a very small proportion of cases of gunshot wounds treated during the War both iodoform, and more particularly bismuth poisoning occurred. In a minute proportion of cases, moreover, the results of bismuth poisoning were disastrous and actually led to death of the soldier.

Those of us who became accustomed to the employment of B.I.I.P. in war wounds believed that such untoward sequelae were the result of improper

technique, particularly in the direction of the employment of too large a quantity of B.I.I.P. or its employment over too large a surface. During the war the author[1] expressed the opinion that if the total surface area of a wound exposed to a proper amount of B.I.I.P. reached 144 square inches, symptoms of important bismuth poisoning were to be expected. As the combined area exposed in cases of multiple wounds among soldiers frequently exceeded this amount, it became necessary to treat only the more seriously contaminated wounds with B.I.I.P. and to employ other methods for the treatment of the remaining wounds. In the opinion of those of us who became enthusiastic in the employment of Rutherford Morrison's procedure, the objections registered to the use of the paste on the grounds of its toxicity were of no more importance than those which might be raised to the employment of morphine, digitalis or strychnine on account of toxic properties exhibited by these drugs when improperly used.

[1] Gurd, F. B. *Lancet*, 1: 731, 1918.

SUMMARY

Although the prevention of mortality is paramount in the treatment of acute appendicitis, shortening of convalescence (more particularly hospital days) and integrity of the abdominal wall are important desiderata.

By the use of a specific technique described in this contribution wound infection with consequent prolongation of active treatment and necrosis of the abdominal wall can be eliminated.

The technique recommended is simple, but must be accurately carried out. Not only is it harmless, but the results would appear to prove that the mortality rate is definitely decreased.

No case of postoperative hernia or of fecal fistula has developed in this series.

REGIONAL ANESTHESIA*

F. D. La Rochelle, M.D. and A. H. La Rochelle, M.D.

SPRINGFIELD, MASS.

In a recent paper Fiedler[1] reports that novocaine is the least and that butyn is the most toxic local anesthetic when injected intravenously in guinea pigs in 2 per cent solution. Butyn is entirely satisfactory, however, in 0.1 per cent solution and this is only one-twentieth as toxic. After using it extensively over a period of several years we believe it is more prompt and that the anesthesia is more satisfactory than that of novocaine. If 7.5 mg. is the toxic dose intravenously this would represent 500 c.c. of 0.1 per cent solution for an adult, and this quantity is seldom necessary although it probably would be safe since the dose of an anesthetic agent is much larger when used subcutaneously and a considerable amount always leaks out of the incised tissues. In our experience we have found that 250 c.c. of 0.1 per cent solution can be used without fear of toxic effect.

We now come to the matter of antiseptic action. In our earlier work we frequently had abscesses develop in the operative field, especially after hemorrhoid operations. While theoretically asepsis is possible enough, practically, it is best to use an antiseptic agent. For this purpose we add rivanol, This drug was originally developed by Morgenroth to sterilize infected foci by saturating the tissues with it. It is non-irritating and non-toxic and a powerful antiseptic. Since using this we have never had an infection develop as the result of injecting anesthetic fluid. To this we add 1 per cent magnesium sulphate to make the solution slightly hypertonic and also for its possible synergistic effect with morphine. Our present solution is as follows:

Butyn	1.0
Rivanol	0.2
Magnesium sulphate	10.0
Aq. Dest	1000.0

Mix, strain and sterilize in autoclave same as dressings. Cap and keep in the dark. This will keep indefinitely.

We believe that no local anesthetic is satisfactory without preliminary narcotization and for this we use sodium bromide in suitable doses. It is best given over a period of several days in 30 grain doses. Dizziness and drowsiness are the symptoms complained of when the full dose is reached. This is usually not necessary, but no apprehension need be felt if they develop. In sthenic individuals we give a dose of veronal at 4 A.M. on the day of operation and thirty to sixty minutes before coming to the operating room we give 1/8 grain of morphine with hyoscine. After this the introduction of a needle should cause no pain; if it does the preparation is not satisfactory and no major operation should be undertaken except in emergencies.

Equipment. We have experimented with apparatus of different sort and have discarded all but a 10 c.c. all metal Pauchet syringe and needles ranging in length from 4 to 10 cm.

Method. Only recently it has been recommended in a paper dealing with operations on the larynx to inject the solution in the proposed line of incision; this should never be done, it should always be injected some distance away and in the path of the afferent nerves, and always in generous quantities. In addition to this if a major operation is planned the large nerve trunks should be bathed in a large quantity of the solution. Never inject the nerves directly but deposit the solution in their immediate neighborhood. The solu-

[1] Fiedler, G. A. Comparative activity of some local anesthetics on mucous surfaces of the urinary tract. Am. J. Surg., N. S., 5:480, 1928.

* Submitted for publication January 18, 1929.

tion will gradually reach them and do less damage. The needle is introduced without the syringe to make sure that a vein has not been entered and the solution is injected as the needle is gradually being withdrawn. Failure to do this might result in injecting a considerable quantity directly into the circulation. For instance, in an operation on the larynx we would inject the cervical plexus on both sides and then block off the field at some distance from the line of incision. In an operation on the breast we would inject the brachial plexus above the clavicle, the intercostal nerves in the posterior axillary line and then block off the skin field. For herniotomy we would inject the lumbar nerves above the iliac crest and then block off the field. Once the injection is completed we discard all apparatus and if the anesthesia is faulty a little ether will usually suffice. We always do this before putting on gloves and draping or painting the field of operation. When this technique is followed carefully it is surprising what can be done without the use of a general anesthetic.

While this method will enable the patient surgeon to do almost any operation one soon learns its limitations.

In operating about the head and neck we have found this technique most valuable. In chest operations it is often life-saving. For abdominal operations it must be supplemented by splanchnic anesthesia and in that case we prefer spinal anesthesia or even ether. For hernia operations it is probably best for strangulated herniae in old people in poor condition, but in a healthy adult when the matter of cure is paramount spinal anesthesia enables one to do a much better repair. In operations about the rectum it is very satisfactory, but again for prostatectomy and major gynecological operations spinal anesthesia is much better and no more dangerous.

In operations on the extremities it is useful, but it must be remembered that local anesthesia is not satisfactory in inflamed tissues. Here gas or ether are much better, especially for short operations.

All in all, that surgeon will get the best result who has at his immediate command every established form of anesthesia and who unhesitatingly adopts the one best adapted to his patient.

NEW INSTRUMENTS

A NEW NEEDLE HOLDER*

A. RAVICH, M.D., F.A.C.S.

BROOKLYN

AFTER many years of hardship with the ordinary type needle holder in deep cavity work, it was thought that, with the introduction by Hugh H. Young of his boomerang needle holder, operative work in deep wounds could be materially facilitated and hastened. Though a very excellent instrument, it is limited in its scope, being useful for deep operative work only. Another drawback is its strong spring which requires considerable muscular power to manipulate. On the other hand, a needle holder which not only serves practically all the requirements of the Young boomerang needle holder without any extra muscular effort, and at the same time can be used as an ordinary needle holder, would fulfill a long felt need.

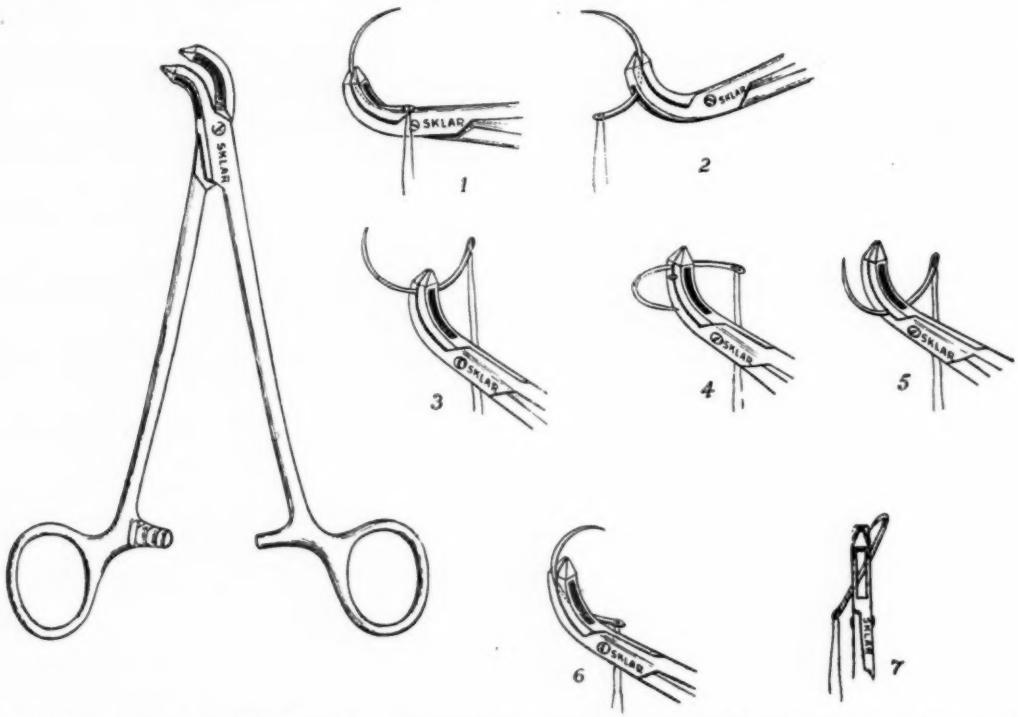

FIG. 1. Author's universal needle holder, showing seven of more common positions a curved needle can be made to assume in its jaws.

The author's needle holder has the conventional handle with an eccentrically placed lock-joint which prevents the handle from springing too far apart. The most important feature of the instrument is the longitudinally fenestrated jaw with which curved needles can be securely grasped at any angle without breaking. The upper jaw is shorter than the lower one and is so arranged as to give good coaptation throughout, thus preventing the

* From the Urological Service of the Jewish Hospital of Brooklyn. Submitted for publication January 14, 1929.

common annoyance caused by the slipping of the needle. The tip of the jaw is tapered and cupped out to strengthen the grip on the needle without breaking it. By shifting the needle at various angles and positions, as shown in the accompanying illustrations, this unique needle holder can be used with equal facility for suturing skin and superficial wounds, as well as in deep wounds, body cavities and orifices.

With little practice this instrument can be of great aid to the laryngologist, gynecologist, rectal surgeon as well as the urologist and general surgeon. With a little manoeuvring many a difficult operation can be materially simplified by its use. The accompanying illustrations show the various details of the instrument as well as most of the positions which the curved needle can be made to assume in its jaws. Straight needles may also be used for superficial work.

A SIMPLE TRANSFUSION TOURNIQUET*

William Z. Fradkin, M.D.

BROOKLYN

BECAUSE of the difficulty in obtaining rapid, firm comfortable, and uniform constriction of the donor's arm, a tourniquet has been devised which

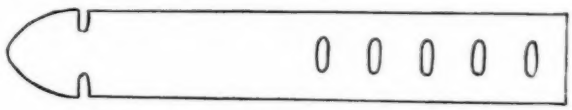

Fig. 1.

is soft, elastic, and needs no knots or buckles for its operation.

It consists of a strip of rubber. One end is square, the other end is tongue-shaped and cut horizontally as shown in Figure I. Near the square end there are five elliptical holes. Figure 2 shows the tourniquet in place around the arm. By pulling on the square end which is free the tourniquet is instantly released.

This tourniquet has the following advantages:

1. It can be easily applied and instantaneously removed.

2. It grips the arm firmly under a constant elastic pressure.

3. It is sterilizable and thus is at the disposal of the operator.

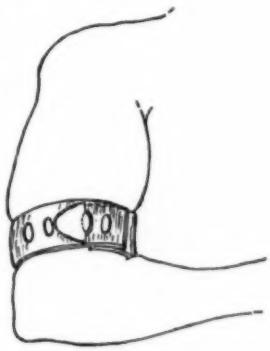

Fig. 2.

4. Its width and elasticity prevents discomfort to the donor.

5. It is manufactured and sold at a very low price.

In addition to transfusions, this tourniquet is useful for emergency measures, for venesections, for intravenous therapy, and diagnostic needs.

* Submitted for publication January 16, 1929.

CASE REPORTS

UNUSUAL FOREIGN BODY WITH VESICAL CALCULUS*

CLARENCE G. BANDLER, M.D., F.A.C.S.

NEW YORK

M. W., An unmarried female aged seventeen years, was admitted to my service at the New York Post-Graduate Hospital in September, 1928. Her chief complaint was "pains on voiding," which had existed for about a year. At this time she complained of constant pain over the bladder region during the previous two months.

While her family history bore no relation to her present condition, her past history revealed that she had had pneumonia when nine years of age, and when thirteen years of age she had been treated in a hospital for "kidney trouble." The treatment consisted of internal medication for a period of ten days. When the patient was five years of age tonsillectomy was performed. Menstruation began at thirteen, was regular every four weeks, and was accompanied by some abdominal pain, the last menstruation having taken place two weeks prior to her admission to the hospital.

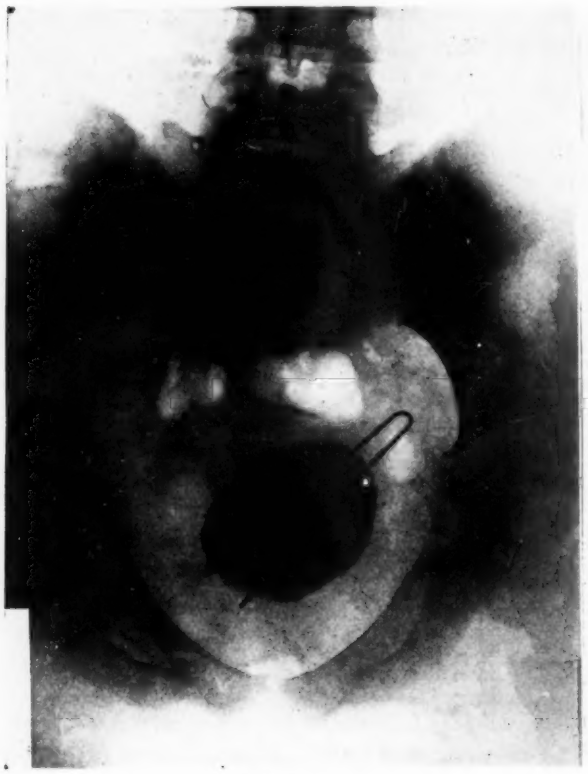

FIG. 1.

FIG. 2.

Present Illness. In November, 1927, this patient first noticed the development of pain on micturition. This pain was referred to the external genitalia, and has gradually but

* Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, Dec. 19, 1928.

progressively increased. The pain was noted toward the end of micturition and would last from ten to fifteen minutes. On several occasions terminal hematuria was observed. Frequency of micturition has been a constant factor, the patient voiding two or three times at night and almost every hour during the day. While there was never sudden cessation of urination, this function has always been slow. During the past four months, patient stated that she had lost 20 pounds in weight, and always felt "weak."

General physical examination revealed a young girl in a fair state of health, whose vital organs exhibited no evidence of disease. Over the lower portion of the abdomen there was general tenderness, more acutely marked to the right of the median line in the suprapubic region. For obvious reasons, no vaginal examination was made, but on bimanual palpation, with a finger in the rectum, a dense mass was definitely palpated in the vesical area. Roentgenographic study of the genito-urinary tract revealed a large, rounded, dense shadow in the bladder area; protruding from opposite poles of this shadow were, apparently, the loop and prongs of a hairpin. The accompanying illustrations clearly delineate the size and nature of this shadow.

Cystoscopic examination showed the bladder contracted about a large stone, which was not movable, but the hairpin, evident in the roentgenograms, could not be observed. Urinalysis revealed an alkaline urine containing a heavy trace of protein with some white blood cells and amorphous phosphatic crystals on microscopic study. Chemical examination of the blood showed no abnormal constituents.

Treatment. Suprapubic cystotomy was performed by me, and a large calculus, which completely surrounded a hairpin except for the terminal exposures of the loop and two prongs, was with some difficulty removed from the bladder. The entire mass was well within the bladder cavity and no vesical perforations were found. Seventeen days after operation the patient left the hospital with the wound entirely healed and apparently completely relieved of all symptoms.

Careful and persistent interrogation of this patient failed to elicit the portal of entrance of the foreign body found in the bladder, but of course a proper history in this respect is rarely obtainable. In presenting the report of this patient with the exhibition of the specimen, as well as the roentgenograms, it is of interest to note that in Follen Cabot's

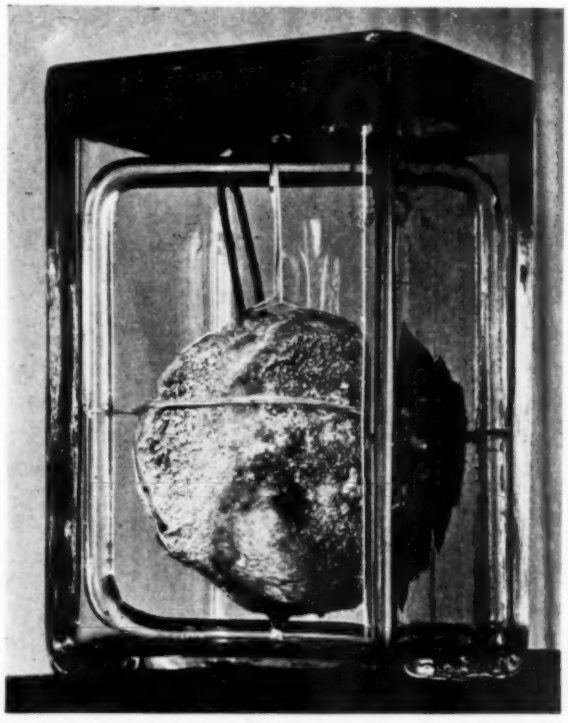

Fig. 3.

small "Compendium of Genito-Urinary Diseases," published over twenty-five years ago, there is a photograph of a similar specimen removed by him, which is almost identical in every respect with that removed from my patient.

DISCUSSION

Dr. H. Dawson Furniss. Some years ago I had a patient, a young hysterical girl, who made a habit of putting foreign bodies in her bladder. Once she inserted a hairpin folded on itself, as though there were four parallel pieces. Later she inserted a glass catheter, the distal end of which broke off and remained in the bladder. This catheter finally became implaced in the hairpin, the long axes of both coinciding. She carried them for sixteen months before incrustation started. Possibly frequent bladder lavage may have been a factor in the delay of incrustation. It was only after a rather large amount had become deposited on the foreign bodies that she permitted me to remove them through a large Kelly speculum.

TERATOMA TESTIS WITH METASTASES CONTROLLED BY IRRADIATION*

ARCHIE L. DEAN, JR., M.D.

NEW YORK

THESE 4 case reports are presented to illustrate the effectiveness of external irradiation upon the teratoid tumors of the testis even in advanced stages of the disease. Each of these men had inoperable metastatic tumors when first seen at the Memorial Hospital. In 2 cases laparotomy had been performed before the diagnosis was ascertained. Examination through the open abdomen revealed the futility of attempting surgical removal.

CASE 1. W. P. K. (M. H. 33171), a clerk, thirty years of age, was referred from the Cornell Clinic March 22, 1924, complaining of a swelling of the left testis of five months' duration. Physical examination revealed a left testis the size of an orange, measuring 21 cm. by 26 cm. in circumferences. It was of elastic consistence throughout and not at all tender. In the left abdomen there was a rounded, hard, fixed, retroperitoneal tumor 10 cm. by 3 cm. in size.

The lungs were apparently free from metastases, Wassermann test negative. The following treatment was given:

a. To the testis 9,000 mc.-hr. at 6 cm. distance by radium pack; 320 ma.-hr. high voltage roentgen rays.

b. To the abdominal metastasis 20,000 mc.-hr. at 10 cm. distance by radium pack; 320 ma.-hr. high voltage roentgen rays through an anterior portal.

At the end of two weeks no abdominal tumor could be palpated. The testis decreased in size steadily. Two months after irradiation a left orchidectomy was performed. At this time the tumor measured 10 cm. and 12 cm. in circumferences.

After histological examination of the removed testis the pathologist reported "syphilis with miliary gummata, collections of lymphocytes, and diffuse fibrous atrophy of tubules." Such a diagnosis being at such variance with the clinical findings, further microscopic study was requested. The revised report on new sections follows: "Several features suggest that one has to deal with the remains of a cellular carcinoma destroyed by irradiation; 1. foci of necrosis surrounded by large polyhedral cells; 2. giant cells lying in small groups of lymphocytes; 3. small groups of large polyhedral cells resembling tumor cells with hyperchromatic nuclei surrounded by lymphocytes. It is therefore concluded that an original cellular carcinoma has largely disappeared under irradiation. This resembles another such case treated a year or more ago."

Since the removal of the testicular tumor the patient has received three cycles of high voltage roentgen-rays to the left abdomen anteriorly and posteriorly and the left groin and scrotum. He is perfectly well and free from all symptoms or signs of disease four years, nine months after the first irradiation.

DISCUSSION

Unquestionably this tumor was a highly malignant embryonal teratoma. Metastasis was early and response to irradiation was prompt. It is this type that is least amenable to surgery.

Usually in the presence of metastases we do not consider orchidectomy, because in these cases it is impossible to assure the patient of benefits to compensate him for enduring even a simple surgical procedure, and furthermore with greater experience in the use of physical agents we find that the local tumor can be managed satisfactorily by external irradiation. In this case the affected testis was removed because the metastatic tumor disappeared completely, and although the primary tumor showed marked regression clinically, we feared regeneration of the car-

* From the Department of Urology, Memorial Hospital, New York. Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, Nov. 21, 1928.

cinoma and further metastases via lymphatic and particularly venous channels.

The question is asked frequently, if external irradiation is so effective, why do we ever perform orchidectomy, particularly in those cases in which no disease can be demonstrated beyond the primary tumor.

I believe we are more conservative than formerly. We no longer remove testes for diagnosis or to learn irradiation effects. In a small group of tumors composed of differentiated adult tissue, irradiation is not effective, and while this type of tumor frequently remains localized for years, metastases may occur. Furthermore the tumor is annoying on account of its size and weight. Therefore it is removed.

We are not as determined upon the removal of the radiosensitive tumors as heretofore because several patients who have refused operation have been carried along in apparently good health for more than five years with irradiation alone. However for the following reasons we recommend irradiation with subsequent orchidectomy in most cases:

1. The operation is simple and easily performed with infiltration anesthesia of ½ per cent novocaine.

2. There is no mortality and the patient is confined for only a few days.

3. The operation removes little testicular tissue that has not already been destroyed by disease. The remaining sound testis furnishes spermatozoa and internal secretions satisfactorily.

4. In spite of many demonstrations of the effectiveness of irradiation, it is difficult not to fear recurrence of a tumor as highly malignant as teratoma testis.

5. If irradiation has been effective and orchidectomy is performed carefully, there is little danger of local recurrence. It has never occurred in a patient of ours.

6. If the *testis* is not removed after the first irradiation, several additional cycles are given to insure complete devitalization of the tumor. In spite of careful protection, the spermatogenic function of the normal testis is destroyed in practically every case.

No doubt when we are able to determine exactly how much irradiation is required to accomplish complete tumor destruction fewer operations will be performed on the highly radiosensitive teratomas. Until more is known it is far safer to err on the side of over treatment.

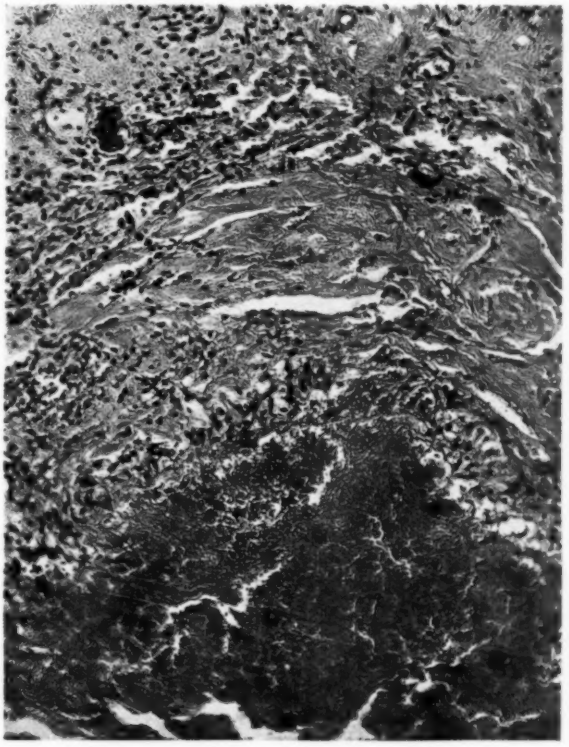

Fig. 1. Case 1. Photomicrograph showing tumor destruction following irradiation.

Case II. M. P. (M. H. 36109), a white clerk, thirty-four years of age, referred from Bellevue Hospital February 25, 1925.

In 1918 patient noticed a swelling of the right testis. By May 1920 it had reached the size of a grapefruit and it was hard. Orchidectomy was performed May 12, 1920. The tumor was a cellular carcinoma. The patient felt well for two years, seven months (January 1923), when he was seized with a very severe pain in the right abdomen. He was rushed to the same hospital and operated upon for appendicitis by the same surgeon who had removed the testicular tumor. At operation the appendix was found normal but a retroperitoneal tumor mass was found 8 in. by 5 in.

in size. This was considered inoperable and the abdomen was closed. After recovery from the operation the patient received one or two superficial doses of roentgen ray and an attempt was made to inject Coley's toxin into the retroperitoneal mass through the abdominal wall. Funds ran low and the man visited Bellevue Hospital whence he was referred to the Memorial Hospital.

On admission February 25, 1925, a huge retroperitoneal mass was found in the right side of the abdomen lying beneath a vertical scar. There were several small firm subcutaneous nodules in the abdominal wall on either side of the scar. No irradiation effects could be detected in the skin. Careful physical examination revealed no signs of local recurrence or metastases other than that in the abdomen.

The following treatment was given:

a. Radium pack of 20,000 mc.-hr. at 10 cm. distance.

b. 320 ma.-min. by high voltage roentgen rays to right abdomen anterior, right abdomen posterior, right groin and scrotum.

Regression of the mass was prompt. In all five roentgen-ray cycles similar to the first have been given; no radium has been applied other than that mentioned above. The dates of the roentgen-ray cycles were March 5, 1925, August 27, 1925, December 8, 1925, May 26, 1926, and February 15, 1927.

The patient now has been well without signs of disease for three years, nine months since the first irradiation.

DISCUSSION

It is not unlikely that a careful examination of the abdomen at the time the testis was removed would have revealed a metastasis. Frequently when a patient presents a testicular tumor of doubtful character abdominal palpation will reveal a metastatic tumor and clear up the diagnosis. Of course the surgeon who removed the primary tumor should have recognized the true nature of the condition when the patient returned with an abdominal mass. Furthermore Coley does not advocate the injection of his toxin into tumors. Treatment by this agent is administered either intramuscularly or intravenously. Attempting to inject toxin into a retroperitoneal tumor through the anterior abdominal approach is awe inspiring. As in the preceding case, we do not know how much unnecessary irradiation was administered. At any rate the man has been relieved to date from a very serious condition.

Case III. G. C. (M. H. 26623), an Italian gardener, thirty-seven years of age, referred to the Memorial Hospital July 1, 1919. There is no history available regarding the symptoms associated with the primary tumor, nevertheless the left testis was removed in 1918 after it had become the size of a large orange. Several months later, March 1919, the patient began to suffer with indigestion and pain in the lumbar region. He found a mass in his abdomen. When he returned to the hospital at which his primary tumor was operated upon, his abdomen was opened and several large retroperitoneal tumors were found. These were considered inoperable, and the man was referred to the Memorial Hospital. On admission, July 1, 1919, a visible tumor mass was present in the right upper quadrant. Palpation revealed that it was hard and immovable, and about 14 cm. in diameter. In the left upper quadrant there was an immovable tumor, stony hard in consistence measuring 8 by 15 cm. in size. There was a scar on the left side of the scrotum and the left testis was missing. No other metastases were found, the lungs were clear. The following treatment was given (radium pack[1] exposures):

July 7, 1919: 12,000 mc.-hr. at 10 cm. distance to left abdomen.

November 7, 1920: 18,000 mc.-hr. at 10 cm. distance to left abdomen.

May 1, 1921: 15,000 mc.-hr. at 10 cm. distance to left abdomen.

Nine low voltage roentgen-ray exposures were given the left abdomen in thirteen days. The factors were 28 ma.-min., 8 in. focal distance, 4 mm. aluminum filter, with a spark gap of 8½ cm.

The patient is now looking and feeling well. He works regularly and there is no evidence of disease eight years, five months after his first irradiation.

[1] The radium emanation pack employed in these cases was 2 mm. of brass in thickness.

DISCUSSION

While there was no histological study made in this case, it probably was an embryonal teratoma. Metastasis was early, growth was rapid, and response to irradiation was spectacular and complete. It is rare to find metastases in the abdomen of the opposite side from that of the primary tumor. In this case the point of origin was the same side as the primary tumor, but the secondary growth became so large that it extended across the abdomen and was visible in this position. All treatment was directed to the left side of the abdomen toward the lumbar nodes from which the tumor developed.

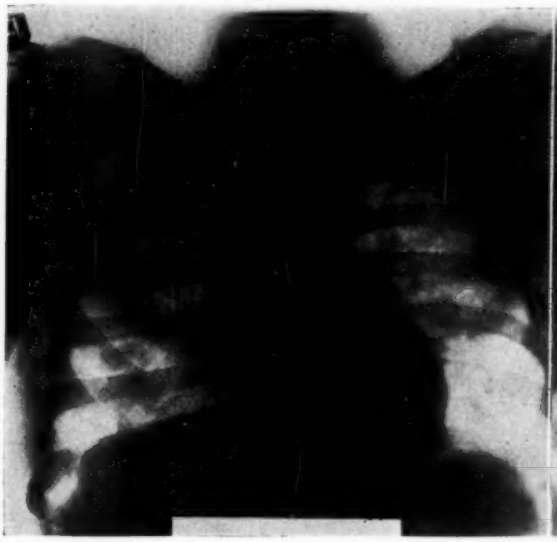

Fig. 2. Case IV. Roentgenogram of chest with lung metastases.

Fig. 3. Case IV. Same as Figure 2, three years after irradiation. There are no signs of metastases.

Case IV. I. N. (M. H. 34735), a negro chauffeur, thirty-eight years of age. In December 1924 patient noticed a painless swelling of the right testis. Two weeks later he was bothered by pain in the back associated with indigestion. The pain was sharp and continuous and it interfered with sleep. Three months later the man noticed that he was becoming short of breath. After losing 36 pounds and becoming quite weak he visited Dr. Ubert C. Vincent, who made the diagnosis of teratoma testis with metastases and referred him to the Memorial Hospital. On admission, May 4, 1925, the patient looked weak and emaciated. He weighed 129 pounds. The right testis was about twice the size of the left, it was stony hard and nodular. There was no tenderness. In the right abdomen there was a rounded, hard, immovable, retroperitoneal mass 5 by 7 cm. in size. In the left supraclavicular fossa there was a firm nodule 2 by 1 cm. in size. A roentgenogram of the chest revealed evidence of extensive metastasis in the lungs.

No operation has been performed. The patient has received 44 high voltage roentgen-ray treatments to the right groin and scrotum, right abdomen anterior, right abdomen posterior, the chest, and the left supraclavicular fossa. Six cycles of therapy have been delivered to each area in which tumor was found. The dates of the cycles were May 1925, January 1926, June 1926, December 1926, March 1927, and August 1927. The man is now apparently well, working regularly, has gained over 20 pounds, and there is no palpable evidence of disease. The right testis is a sclerotic nodule 2 by 1 cm. in size. Roentgenograms reveal no signs of metastases in the lungs. He has been relieved three years six months.

DISCUSSION

While there has been no histological diagnosis made in this case, there can be little doubt that we were dealing with another of the cellular, embryonal teratomas which grow rapidly, metastasize early and are remarkably radiosensitive.

This case illustrates the desperate condition of many of our patients when they are first seen. In every case, if the patient is not moribund, treatment is given. Even with extensive lung metastases and generally low vitality irradiation in our hands has not made the patient weaker.

It would not seem unreasonable to think that repeated irradiation to metastatic abdominal tumors would injure the kidney of that side. The writer has attempted to answer this question by performing cystoscopic examinations on a series of patients (cases I, II, and IV were so examined). Functional studies together with pyeloureterograms have shown no abnormalities to date.

LEIOMYOMA OF THE URINARY BLADDER*

LEONARD PAUL WERSHUB, M.D.

NEW YORK

IN reviewing the literature of benign non-papillary tumors of the bladder, it is interesting to learn of the relative infrequency of such pathology. Under "tumors of the bladder" in the card index system of the Academy of Medicine, little mention is made of this type of tumor, and for reference material one must seek other sources. Assuming the relative infrequency of certain benign tumors of the bladder such as myxoma, myoma, lipoma, fibroma or leiomyoma it is nevertheless surprising to note the almost negligible number of accounts of such tumors being observed through the cystoscope. That these tumors are rare in vesical pathology is shown by their relative absence in the literature, where they usually appear as findings of the post-mortem table or in reports of removal of supposed malignant tumors and subsequent microscopical classification as benign tumor growth.

Koll[1] in reporting a case of fibroma of the bladder, in 1922, and in a most careful review of the literature up to that time, summarizes 38 cases under the heading of benign non-papillary tumors of the bladder. Of these, 4 were fibromata, and 34 tumors containing smooth muscle. Twenty-nine cases were reported as to sex and age of patient, size and location of tumor and histological diagnosis. Only 4 cases were true fibromata and it is interesting to note in this respect that these were only diagnosed as such at the autopsy table. Few additional data have been contributed since Koll's report. A subserous myoma weighing over a pound has been described by McNally.[2] Kidd and Turnbull[3] report a case of pedunculated angiomyoma and Kostjurin[4] a small fibromyoma. Quite recently Stevens[5] reported a case of tumor of the bladder wall, observed through the cystoscope and its subsequent removal with histological diagnosis of leiomyoma. That the diagnosis can be made preoperatively aided by the cystoscope is borne out by the following case report:

CASE I. 28–615. A. J. female, aged forty-two, colored, single, houseworker. When first seen complaint of patient was dysuria, frequency and accompanying history of pyuria and hematuria. This condition was first noticed in July, 1927, following a fall, with trauma to the left side of the abdomen. About two weeks after the injury, the patient first noticed blood in her urine, which at first appeared blood tinged and later contained shreds of clotted blood. There was great desire to void, but resulting only in the passage of a few drops of bloody urine, with great difficulty and pain. Physical examination was otherwise negative. Past history was irrelevant. Cystocsopic examination in November, 1927, revealed marked

* From the Department of Urology, N. Y. Homeopathic Medical College and Flower Hospital. Submitted for publication January 12, 1929.

induration of the floor of the urethra just behind the meatus, which was contracted. There was a moderate trigonitis. Ureteral apertures were easily visualized and normal in appearance. Intravenous injection of indigo-carmine appeared equally in four minutes with equal concentration. The urine was cloudy with shreds.

Fig. 1. Low power photomicrograph.

Fig. 2. High power photomicrograph.

Second cystoscopic examination in December, 1927, showed definite improvement in the trigonitis. The right and left ureteral orifices were visualized without any difficulty, and specimens obtained from both kidneys showed equal area content. These specimens failed to show any bacterial growth.

Two months after the first examination, cystoscopy revealed a tumor formation in the region of the left trigone, 2 cm. in diameter and ½ cm. in height. This was covered by a ridged and edematous mucosa. The growth was not pedunculated. These findings gave us the first clue as to the neoplastic nature of the disease process present in the bladder. At this examination, the right ureteral aperture had a normal eflux and was clearly seen, but the left aperture could not be visualized, apparently being obscured from view by the tumor mass.

The patient reported for examination one month later, and reported that in the interval additional symptoms had developed, i.e. dysuria and frequency (eight to ten times daily, and nocturia three to four times). A specimen of urine secured by catheterization appeared cloudy. Cystoscopy at this time revealed the right half of the bladder to be approximately normal with some redness of the right aperture. On the left side of the bladder extending from about the junction of the inner third of the roof to a point slightly beyond the midline of the trigone was an irregular tumor mass which appeared more defined than on previous examination. Its surface was irregularly smooth, reddish in appearance, with scattered grayish areas. The mucosa surrounding the base of the tumor was very much reddened and edematous. The tumor mass lay over the left ureteral aperture and extended slightly posterior to the interureteric line and almost to the internal sphincter. The tumor suggested a benign growth, probably a myoma or fibroma. Efforts at cathetrization of the left ureter which could not be visualized failed. In view of these findings a tentative diagnosis of benign neoplasm of the bladder was made. It was sug-

gested that the patient be admitted to the hospital for a suprapubic cystotomy to determine the exact nature of the growth and that she be treated accordingly.

Subsequent examinations at the hospital showed following reports. Repeated examinations of the urine were essentially negative with the exception of a faint trace of albumin, occasional crystals of triple phosphates, scanty pus corpuscles, with abundant red blood cells. Blood count on February 15 showed a hemoglobin of 75 per cent (Sahli), color index 0.93, red blood cells 4,035,000 per c.mm. and white blood cells 7200 per c.mm (neutrophiles 48 per cent, lymphocytes 52 per cent. Blood chemistry on the same date revealed a non-protein nitrogen 27.3 mg. per 100 c.c., creatine 1.15 mg. per 100 c.c. and sugar 95.2 per 100 c.c., carbon dioxide 48 per cent. Phenolsulphonphthalein test in the first hour revealed 15 per cent and in the second hour 35 per cent. The Wassermann reaction was negative.

On February 16 under general anesthesia suprapubic cystotomy was performed by Dr. Louis Rene Kaufman. A pedunculated tumor, irregularly oval in shape, measuring about 2 cm. in diameter, was found on the left side of the bladder wall near the trigone. This was found 2 cm. internal to the sphincter. The mucosa was incised and the tumor shelled out easily. The base of the tumor area was treated with electric cautery. A suprapubic tube was inserted into the bladder; the anterior wall of the bladder sutured with interrupted catgut; the remainder of the closure was carried out in routine manner. The suprapubic tube was removed on the ninth day postoperative, and the patient discharged from the hospital nineteen days after admission.

Pathological report of specimen by Dr. W. E. Youland of the Department of Pathology. "Specimen consists of a small ovoid mass about 2 cm. in diameter and apparently completely encapsulated. On section the tissue was pearly white, firm and glistening. Microscopically the tissue was made up of irregularly arranged strands of large cells, having elongated nuclei together with abundant fibrillar cytoplasm. The cells presented no distinctive arrangement or fascicle formation but ran in every direction with considerable interlacing. There was at one point from the surface of the section an area of ulceration with an underlying layer of monocytic infiltration including a small proportion of leucocytes. The tissue as a whole also shows a slight degree of cellular infiltration." Subsequent pathological diagnosis was made of leiomyoma of the urinary bladder.

On March 6 the patient reported for follow-up examination. Her complaint at this time consisted in the main of frequency (which rapidly cleared up with bladder irrigations); there was no nocturia, hematuria or dysuria. Urine by catheter showed a few flakes but was grossly clear. This specimen was negative to bacterial growth. With a distention of about 100 c.c. of boric-acid solution, there was seen at the vault a triangular dark, red area, about ½ cm. in length and less in transverse diameter; this was approximately at the site of the suprapubic operation. The right half of the bladder wall was normal. The right aperture was clearly seen and was negative pathologically. The left aperture presented as a round, reddened opening with a somewhat thickened roof of normal mucosa. Just behind the aperture and just above it was an area about 2 cm. in diameter, which presented discrete, reddened areas, varying in size from a few millimeters to ½ cm. The largest area was covered with a grayish exudate. In front of the left aperture, the mucous membrane is somewhat reddened but smooth and without exudate.

I am greatly indebted to Dr. Louis Rene Kaufman from whose service this case was taken, for permitting me to report it.

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EPITHELIOMA OF THE PENIS*

GEORGE A. WYETH, M.D.

NEW YORK

I AM presenting this case, not as a cured case of epithelioma of the penis but as a rather extensive one which has been somewhat relieved by endothermy.

A young married man of forty-four years came under my care one and a half years ago with the history that about six months previously he had noted what he thought was a boil on the under surface of the head of his penis. This did not "come to a head" but began to grow rather rapidly and was about the size of an English walnut when he consulted a genitourinary specialist who *cut* out a piece for examination and a diagnosis of benign papilloma was made. Immediately following this biopsy the lesion grew very rapidly and had progressed to the size of a large orange when I first saw it in June, 1927. It was an extremely large cauliflower growth springing from the under surface and involving practically the entire shaft of the penis. Wassermann reaction was negative. The patient was bedridden and somewhat incapacitated by the large, painful, tender organ. It was infected, foul and malodorous. The patient was anemic, somewhat cachectic and badly run down. He was passing no urine by meatus; in fact, it was impossible to find the meatus, and the urine trickled out through three sinuses on the under surface. A bilateral, polyganglionic inguinal enlargement was present and the case was considered inoperable from the standpoint of scalpel surgery.

With new methods we are learning to do new things for the benefit of advanced cases of cancer that we should not have attempted five years ago. With no promise except to remove the offending organ, the patient was etherized and a two-stage operation was begun by amputating the penis at its extreme base with the endotherm knife and coagulating current. The urethra was sutured to the skin and healing was without incident. The pathology proved to be a Grade 2 papillary epidermoid carcinoma. Inflamed glands of both groins reduced themselves except for two on the right side and three on the left which remained palpable. These were removed by the endotherm knife and desiccating current four weeks after the first-stage operation. I feel very strongly on the advantages of a two-stage operation on these badly infected, advanced cancer cases and I believe that had I at the first operation opened the entire circulation by removing Nature's barriers, the lymphatic glands, I should have lost my patient with an acute toxemia. We have learned this from our advanced breast, tongue and floor-of-the-mouth cases. These glands showed lymphadenitis with simple hyperplasia and showed no evidence of carcinoma. The wounds healed kindly; the patient gained rapidly in weight and resumed his occupation, reporting for regular observation for about nine months. He then became careless and I did not see him for several months when he reported to me in August of this year with a distinct recurrence on his tiny stump. He had two palpable glands in the left groin and one in the right.

The patient was again etherized and a continuous incision was made with the endotherm knife beginning at the outer edge of the left inguinal region over the pubes to the outer margin of the right inguinal region. A curved incision was then made downward into the perineum, going through the posterior portion of the scrotum. This was continued upward and outward on the opposite side to the outer area of the left inguinal region or the beginning of the first incision. The skin was then elevated and working downward the two glands were removed in toto with a single gland of the right side and the large triangular area. In removing this area the incision was carried downward from beneath the pubic arch and all attachments freed from both rami of the pubes. The urethra was dissected out, severed and sutured to the skin in the perineum. Artificial pockets were made between the abdominal fascia and fat and the testicles were transplanted to these and held by retention sutures of catgut. The wound was then closed with drainage.

The two points I would like to make are:

1. The futility and *danger* of cutting off with the scalpel a piece of tumor for

* Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, Dec. 19, 1928.

biopsy. We are now taking all biopsies for immediate frozen section with the endotherm knife.

2. That even in advanced cases of cancer sometimes a great deal can be done for their relief.

CASE REPORTS BY DR. B. S. BARRINGER*

NEW YORK

CARCINOMA OF THE PROSTATE CONTROLLED SIX YEARS BY INTERSTITIAL IRRADIATION

THIS patient, a physician, presented the following history:

He was operated upon in December, 1921 on Dr. Beer's service at the Mt. Sinai Hospital for a urinary retention. The preoperative diagnosis was hypertrophy of the prostate. On sectioning the prostate the diagnosis of carcinoma was made, the carcinoma extending to the edge of the section. This diagnosis was confirmed by Dr. Ewing.

I believe that Dr. Aschner from the physical findings, induration of the prostate and periprostatic region, thought that the carcinoma had not been entirely removed. That certainly was my impression.

I radiated the prostate, the periprostatic and the supraprostatic regions by means of radium needles inserted through the perineum. He had about four treatments. There was no deep roentgen-ray therapy. It is now seven years since his first irradiation.

By rectal examination his prostate feels scarred and sclerotic, but there is nothing that I could definitely identify as carcinoma.

He is in active practice and doing a full day's work.

INOPERABLE INFILTRATING CARCINOMA OF THE BLADDER: TWO CASES

The 2 following cases are reported because both of them had inoperable infiltrating bladder carcinoma and both have been controlled for over seven years by radon implants.

CASE I. The patient was first seen in 1920, nearly eight years ago. He had a history, dating back three months, of frequency and burning on urination, and later hematuria. On the anterior bladder wall, coming in contact with the ureters, was a sloughy tumor, with a base 4 × 3 cm. touching the internal urethral orifice. I did a suprapubic section. The tumor proved to be an infiltrating epidermoid carcinoma (pathological examination by Dr. Ewing). His tumor was implanted with the old-fashioned glass seeds of radium. He had a pretty large dose, 21 bare tubes of radium, and in addition 433 mc. hours of screened radium. He went on fairly well but had a large slough at the tumor site.

In 1922 I removed a stone from the bladder formed on the slough. He had no tumor. Since then he has gone on very well, has had no symptoms, and as far as I can see he is cured. He is doing a full day's work after eight years, despite the fact that squamous carcinoma is the most radio-resistant type and one of the most malignant types.

CASE II. This was a man seventy-two years old, who came to us on June 14, 1921, with a history of a year's hematuria as practically the only symptom, although he had some dysuria. The whole right side of the bladder was filled with tumor. We did a suprapubic cystotomy, and Dr. Ewing returned a diagnosis of papillary carcinoma of the bladder. We put it down as infiltrating carcinoma because of the intensive induration at the base of the tumor. He also had implantations of unscreened radium. He had twenty bare tubes placed in the tumor base besides screened radium, 663 mc. hours. The growth was estimated to be 5 × 6 cm., practically the entire half of the bladder.

He has been cystoscoped several times since. His bladder is clean. When I saw him about two months ago he was in good health.

He went through a stormy time after the cystotomy. He was rather fat and not a good risk. He is at present doing a full day's work. It is now seven and a half years since the original implantation in the bladder, and he is over seventy-eight years of age.

* Read before the Section of Genito-Urinary Surgery, N. Y. Academy of Medicine, Nov. 12, 1928.

The American Journal of Surgery

Publishing the Transactions of THE AMERICAN ASSOCIATION FOR THE STUDY OF GOITER; THE PACIFIC COAST SURGICAL ASSOCIATION, THE NEW YORK UROLOGICAL SOCIETY; SECTIONS OF SURGERY, GENITO-URINARY SURGERY AND ORTHOPEDIC SURGERY OF THE NEW YORK ACADEMY OF MEDICINE; LOS ANGELES SURGICAL SOCIETY, ETC.

Editor: THURSTON SCOTT WELTON, M.D., F.A.C.S., NEW YORK

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EDITORIALS

HISTORICAL INTRODUCTIONS

IT has been a noticeable fact in recent medical and surgical literature that authors have started their writing with a brief resume of the historical aspects of the topic to be discussed. This is a pleasant and worthwhile innovation.

Recently a physician of national fame said the profession was entering the cultural stage of its evolution. Within the past few months the circulation of the *Annals of Medical History* has had a healthy growth. In many of the national and local journals devoted to the various departments of medicine are to be found abstracted articles dealing with medical history. The new books devoted to medical biography and the historical background of physic fill a much felt desire on the part of an increasingly large number of our fellow practitioners.

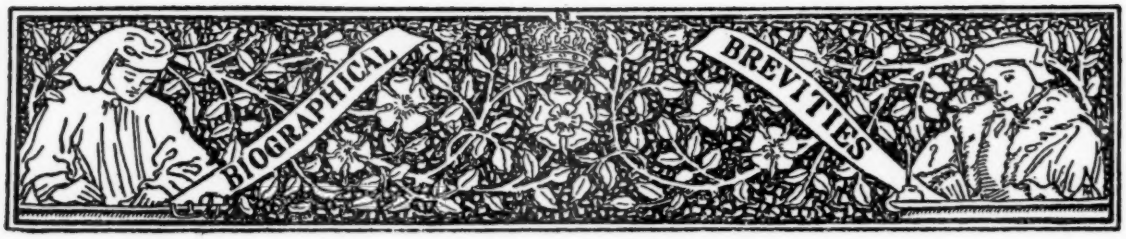
It has been stated that no one reaches the heights of his profession, whether it be medicine, law, theology or architecture, without having become, in a sense, an authority on the history of his calling.

And so we urge him who reads these lines to take the hint thrown out and, in the future, when preparing an essay for publication, to collect all the historical facts possible that bear on the topic at hand and, in a terse manner, offer them as an introduction. T. S. W.

ANNOUNCEMENT

THE Executive Council of the American Association for the Study of Goiter has instructed me to inform you that a prize of three hundred dollars ($300.00) and a medal of honor will be awarded by the Association to the author of the best essay based upon original research work on any phase of goiter, presented at their annual meeting at Seattle, Washington, in September 1930.

Competing manuscripts must be in the hands of the Corresponding Secretary, J. R. Yung, M.D., Terre Haute, Ind., by July 4, 1930, so that the award committee will have sufficient time to thoroughly examine all data before making the award.



"GRAVES' DISEASE."

HIS father a Dublin clergyman, Robert James Graves was born in 1796. He took his medical degree in 1818. He followed this, as was usual with many of his time, by a tour of the continent. While on this journey he had enough adventures to satisfy several characters from the pen of a Conrad or a Kipling. He was arrested as a German spy in Austria. He successfully quelled a mutiny on board the ship on which he was a passenger in the Mediterranean, took command and, by his daring and nerve, saved the ship from being wrecked. In 1821 he returned to Dublin. At once he became as active as the proverbial bee. He was made chief physician to the Meath Hospital. He was one of the founders of the Park Street School of Medicine. He introduced new methods of clinical teaching common to continental teachers, the feature of which was to have advance students handle and report on clinical cases. He ended the abuse of poor patients, dependent on charity, who had to suffer from the borish, brutal Irish physicians of the day. He published his Clinical Lectures in 1848. These lectures contained much matter new at that time, such as the "pin-hole pupil," counting the pulse by the watch, and throwing into the discard the time-worn treatment of fevers by lowering them. Graves was almost a fanatic concerning therapeutic innovation. He requested that his epitaph read, "He fed fevers." Between 1843 and 1848 he published essays on scleroderma, erythromelalgia and angioneurotic edema. He published his enduring account of exophthalmic goiter, which pathological condition still is known by his name, in 1835.[1]

Graves was tall, swarthy, and had a distinguished manner. He had a habit of sarcastic speech but was generous and warm hearted. He died in the most active period of his labors in 1853, at the comparatively early age of fifty-seven years.

T. S. W.

[1] *Lond. M. & S. J.*, 1835.

ROBERT JAMES GRAVES
[1796-1853]

The American Journal of Surgery
N. S. Vol. VII, August, 1929

[From Fernelius' Universa Medicina, Geneva, 1679.]

BOOKSHELF BROWSING

A PAPER THAT INAUGURATED A NEW SURGICAL ERA

IN this age of hurry, most of us an hour behind mapped out schedules of work, it is not unusual for the majority to run as they read and to accept what is offered on a printed page without seeking the original.

The Lister centenary was celebrated in 1927. It is not the purpose of this trifle to restate facts that have been retold hundreds of times in as many scientific periodicals and books.

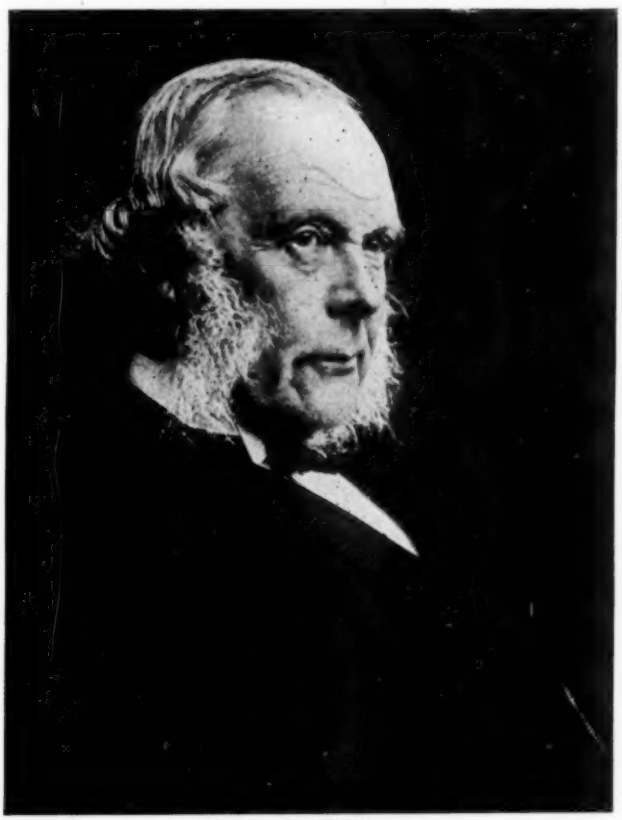


FIG. 1. Lord Lister.

However, every time one enters an operating room and contemplates the surgical miracles that are performed, in

truth merely commonplace routine surgical manouvres, he is forced to let his mind go back to that time when to undergo any surgical operation, no matter how slight or minor, was to gamble with death. Before the time of Pasteur and Lister surgery was a serious problem to both physician and patient.

Then it came to pass that in France Pasteur gave to the world his brilliant discoveries. In Great Britain Lister put Pasteur's discoveries to practical application in his operating room and thus caused to be born the modern era of surgery. During the past fifty years surgery has made far greater advances than it did during the preceding twenty centuries. Lister, ridiculed at first by his colleagues and not given serious consideration at the time, opened the door and showed the way.

While looking through some old copies of the *Lancet*, we chanced upon the issue of March 16, 1867. On page 326 the running head reads, "New Method of Treating Compound Fracture, Abscess, etc."

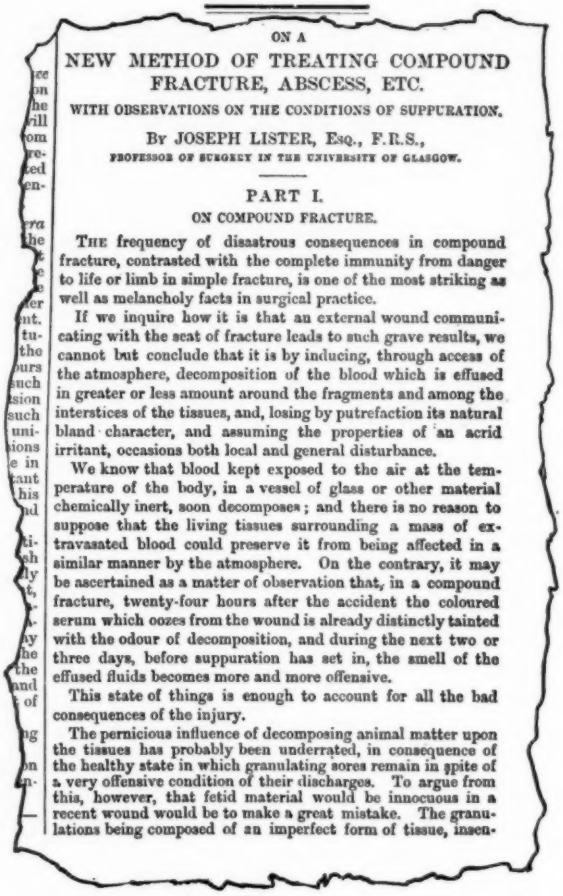
In the second column, half way down the page is a modest heading:

On A
New Method of Treating Compound
Fracture, Abscess, Etc.
With Observations on the Condition
of Suppuration.
By Joseph Lister, Esq., F.R.S.
Professor of Surgery in The University
of Glasgow.

Lister's writing was published in several parts. In it he gave his reasons for attributing infection to germs carried by the dust-laden air and his method of carbolic acid treatment. For the most part the article is composed of case reports proving his points.

This series antedated his article, "On the Antiseptic Principle of the Practice of Surgery," which the more firmly put Lister on record as the advocate of his then original method of surgical antisepsis.

In the first article of the *Lancet*, which strictly marks the first of Lister's writings on antisepsis, the following appears:



ON A

NEW METHOD OF TREATING COMPOUND FRACTURE, ABSCESS, ETC.

WITH OBSERVATIONS ON THE CONDITIONS OF SUPPURATION.

By JOSEPH LISTER, Esq., F.R.S.,
PROFESSOR OF SURGERY IN THE UNIVERSITY OF GLASGOW.

PART I.

ON COMPOUND FRACTURE.

THE frequency of disastrous consequences in compound fracture, contrasted with the complete immunity from danger to life or limb in simple fracture, is one of the most striking as well as melancholy facts in surgical practice.

If we inquire how it is that an external wound communicating with the seat of fracture leads to such grave results, we cannot but conclude that it is by inducing, through access of the atmosphere, decomposition of the blood which is effused in greater or less amount around the fragments and among the interstices of the tissues, and, losing by putrefaction its natural bland character, and assuming the properties of an acrid irritant, occasions both local and general disturbance.

We know that blood kept exposed to the air at the temperature of the body, in a vessel of glass or other material chemically inert, soon decomposes; and there is no reason to suppose that the living tissues surrounding a mass of extravasated blood could preserve it from being affected in a similar manner by the atmosphere. On the contrary, it may be ascertained as a matter of observation that, in a compound fracture, twenty-four hours after the accident the coloured serum which oozes from the wound is already distinctly tainted with the odour of decomposition, and during the next two or three days, before suppuration has set in, the smell of the effused fluids becomes more and more offensive.

This state of things is enough to account for all the bad consequences of the injury.

The pernicious influence of decomposing animal matter upon the tissues has probably been underrated, in consequence of the healthy state in which granulating sores remain in spite of a very offensive condition of their discharges. To argue from this, however, that fetid material would be innocuous in a recent wound would be to make a great mistake. The granulations being composed of an imperfect form of tissue, insen-

FIG. 2.

"Turning now to the question how the atmosphere produced decomposition of organic substances, we find that a flood of light has been thrown upon this most important subject by the philosophic researches of M. Pasteur, who has demonstrated by thoroughly convincing evidence that it is not oxygen or to any of its gaseous constituents that the air owes this property, but to minute particles suspended in it, which are germs of various low forms of life, long since revealed by the microscope, and regarded as merely accidental concomitants, resolving the complex organic compounds into substances of simpler chemical constitution, just as the yeast plant converts sugar into alcohol and carbonic acid.

"Applying these principles to the treatment of compound fracture, bearing in mind that it is from the vitality of the atmospheric particles that all the mischief arises, it appears that all that is requisite is to dress the wound with some material capable of killing these septic germs, provided that substance be found reliable for the purpose, yet not too potent as a caustic . . .

"My attention having for several years been directed to the subject of suppuration, more especially in its relation to decomposition, I saw that such a powerful antiseptic (carbolic acid) was peculiarly adapted for experiments with a view of elucidating that subject, and while I was engaged in the investigation the applicability of carbolic acid for the treatment of compound fracture naturally occurred to me.

"My first attempt of this kind was made in Glasgow Royal Infirmary in March, 1865, in a case of compound fracture of the leg. It proved unsuccessful, in consequence, as I now believe, of improper management; but subsequent trials have more than realized my most sanguine anticipations."

We reproduce a facsimile page of the first installment of Lister's early epoch-making contributions to the surgical literature. The reader will be impressed with the modesty of its appearance. We wonder how many who read these early articles, sixty odd years ago, realized they were to be the means of inaugurating a new surgical era. T. S. W.

BOOK REVIEWS

This[1] is the second of Harper's series of medical monographs and, as was to be expected of any monograph by this gifted author, it is full of meat and may be read to advantage by all physicians. The author states in his preface: "The chief excuse for this little volume is that it is an attempt to present the practical phases of the complex in a sufficiently clear manner to be understood by all, and particularly to stress the subject of treatment. It is not the treatment of the condition but rather that of the individuals who suffer from it which chiefly interests the writer." This last sentence might well be applied by all physicians in practically all pathological conditions that they have to face.

The new volume of the Mayo Clinic Monographs by Willius on "Clinical Electrocardiograms"[1] is a splendid production which, according to the author's preface, "has been devoted entirely to the subject of reading of the records themselves and their clinical significance. There has been no attempt to discuss the technic of electrocardiography, the preparation of records, theory, or the many controversial questions." The author's purpose has been fully accomplished and a study of the records published cannot but be instructive to anyone interested in electrocardiography. The reproduction in line instead of half tone, as is done in most of the other books, makes for greater ease of reading and it is hoped that other publishers will profit by the example set by Messrs. Saunders in this instance.

The annual appearance of this volume[2] represents to the older men the return visit of an old friend. Would that more of the writers of today availed themselves of this volume, thereby avoiding much unnecessary repetition. The present volume, as usual, shows the most careful editing and is splendidly illustrated, including numerous colored plates. Medicine today is really too complex to have justice done to the year's progress in a single volume. This makes it all the more remarkable to see the thoroughness with which the Editors have covered the almost unlimited ground and still kept the volume under 600 pages. A splendid index renders the volume extremely valuable for quick reference. Full justice is dohe to the English and American literature of the past year though the references to German and French journals are not as profuse as formerly.

Here is a reprint of two outstanding articles[3] in Nelson's Loose-Leaf Living Medicine. Bound

[1] Angina Pectoris. By Harlow Brooks, M.D. N. Y., Harper & Bros., 1929.

[1] Clinical Electrocardiograms; Their Interpretation and Significance. By Frederick A. Willius, M.D. Phila., W. B. Saunders Co., 1929.

[2] The International Medical Annual. Ed. by Carey F. Coombs, M.D., F.R.C.P., and A. Rendle Short, M.D., F.R.C.S. N. Y., William Wood & Co., 1929.

[3] Diseases of the Thyroid Gland. By Nellis Barnes Foster, M.D., and Eugene H. Pool, M.D., N. Y., Thomas Nelson & Sons, 1929.

in flexible leather in pocket format, it is the type of monograph of which it would be desirable to see a great many more published in this country. Without loss of words Doctors Foster and Pool have covered the subject in a complete and up-to-date manner. For "reading up" on the subject there is no better material on the market. It is to be hoped that the success of this reprint will be such as to warrant the publishers in issuing a long series of similar volumes.

Here[1] is a fascinating treatise which should prove of great interest to the orthopedic surgeon. Also, it is instructive and good reading to anyone who is a physician.

Not so many years ago surgery offered, at best, a very uncertain hope to anyone with an ankylosed joint. Today only comparatively few surgeons are capable of getting uniformly satisfactory results from operations in these cases. W. Russell MacAusland has done much original work in this field, and the writer has a vivid recollection of a paper read abroad six years ago by MacAusland on this topic.

In this present work of only 252 pages the authors have proved the point that arthroplasty has become a standardized form of treatment for mobilization of ankylosed joints. Throughout the work credit is given to all experimenters who have contributed to the process of standardization. The methods of operators that are giving consistently good results have been described in detail with illustrative cases. Bibliographic notes supply definite information as to the specific tests cited.

A notable contribution to the surgical literature of the times. We most earnestly recommend it.

The all-important subject of Peptic Ulcer is treated in this volume[2] with typical German *gruendlichkeit* and the closely printed bibliography of 80 pages makes this book a reference work that is indispensable to every surgeon. An evidence of the completeness of the study made by the author is perhaps best shown by the fact that he is not satisfied to begin with Cruveilhier, who described the first clinical picture of peptic ulcer based on pathological studies, but traces back through the literature evidences of peptic ulcer not recognized as such as far back as 1550, and from that point on the literature is considered right up to 1928 with due recognition of American and English work on the subject. To all of this is added a study of the clinical material in the famous author's own clinic in Bonn. The lack of an index is the only thing that the most carping critic could find to cavil at, and the omission of this is to be blamed on German custom rather than on the individual author. Truly a book that no German-reading surgeon should do without.

A little book[1] of 100 pages on preparation and after treatment in surgical operations. This little pamphlet should be in the hands of all young surgeons and many an experienced practitioner will find it to his advantage to refresh his memory by a rapid survey of this little primer.

One hundred and sixteen pages on the possible accidents the surgeon faces in doing a cholecystectomy.[2] The surgeon handling such cases will find much wisdom in these pages and will find their perusal well worth while. Warning against possible accidents can never be made too emphatic. If this book succeeds in its effort to prevent avoidable trauma in cholecystectomy its publication will be amply justified.

This volume[3] presents a collective study of every phase of joint diseases from the viewpoint of roentgenology, orthopedics, endocrinology, metabolism, pathological anatomy, bacteriology and serology. A large order for one man! A fact which the author duly faces in his preface where he points out the practical impossibility of, at the present time, producing a volume on this subject with every chapter covered by a specialist. Feeling the need of a complete reference work he has set himself the task of writing such a volume based on a complete study of the literature supplemented

[1] The Mobilization of Ankylosed Joints by Arthroplasty. By W. Russell MacAusland, M.D., and Andrew R. MacAusland, M.D. Phila., Lea & Febiger, 1929.

[2] Die Pathogenese des Peptischen Geschwurs des Magens und der Oberen Darmabschnitte. By Dr. Erich Freiherr V. Redwitz. Stuttgart, Ferdinand Euke, 1928.

[1] Die Vor- und Nachbehandlung bei Chirurgischen Eingriffen. By Dr. M. Behrend. Ed. 2. Berl., Julius Springer, 1929.

[2] Les Accidents de la Cholecystectomie. By Serge Huard. Paris, Masson et Cie, 1929.

[3] Gelenkerkrankungen Einfuhrung in die Pathologie und Therapie. By Ernst Freund. Berlin, Urban & Schwarzenberg, 1929.

by his own clinical work in the clinics of Profs. Wenckeback and Kovacs of Vienna with the pathological phases supervised by Prof. Erdheim. The book presents a complete picture of the present status of the subject supplemented by a splendid bibliography which simplifies further reading. The book is divided into 14 chapters with about seventy pages devoted to treatment. Here is a ready reference volume that should prove invaluable to every surgeon and general practitioner. It is a book that should be translated into English as there is nothing else of just this kind available.

"All You Need to Know About Gastroscopy in a Nutshell" would be a suitable title for this book.[1] Eliminating the technical details so boring to the average medical man, the author devotes this hundred-page monograph entirely to the place of gastroscopy in diagnosis. The book offers an eleven-page bibliography which gives an indication of the importance of the subject. The forty-six illustrations are well selected and reproduced with the excellence we have come to expect from the house of Springer.

One hundred small pages,[2] giving an outline of the operations the general practitioner can handle in his own office or in the home of the patient—limited, in reality, to emergency operations. A convenient handbook for the very young surgeon.

We disagree with the opening statement of Dr. Doughty's Preface:[3] "One is tempted to regret the title of this book. The general reader is apt to note it and pass on. It seems to indicate no more than another of those technical works, which must form a part of the library of every well-equipped physician."

Rather than regretting this title, we find it stimulating; and far from being inclined to "note it and pass on," we were intrigued by it, to the extent of reading more of these two volumes than the technical reviewer is generally wont to do.

The author's Foreword begins with the statement: "In no country is the history of medicine so well preserved as in Canada; in no country is the story so all-absorbing, so replete with striking incident."

We agree with the facts, but take issue with the comparison. Canadian medical history *is* interesting, but so, we insist, is *all* medical history. Four centuries are not long in history of medicine, but when it is realized that our sister Dominion already has four hundred years of history behind her, it seems long indeed—and interesting, every year of it.

The scope of the work of these two volumes is perhaps best shown by the six parts into which it is divided: I. Epidemics of Disease; II. Pioneer Physicians; III. Medicine and Surgery; IV. Public Health; V. Medical Schools; VI. Hospitalization. To us, the most interesting section, from the narrative point of view, is the record of pioneer physicians. Pioneers indeed were men like Dr. Bonnerme, the first physician to visit Quebec, who, according to the author, "narrowly escaped hanging for being implicated in a plot with members of Champlain's crew against the life of Champlain."

As is essential in any work attempting completeness as does this one, much space is devoted to dry statistics and records. Fortunate however, is he who does research in medical history, to have at hand such a compact and complete assemblage of all the available data on the Medical history of Canada.

[1] Die Gastroskopie im Rahmen der Klinischen Magendiagnostik. By Dr. Kurt Gutzeit. Berl., Julius Springer, 1929.

[2] Was Kann und Wann Muss der Praktische Arzt Operieren? By Richard Muhsam. Leipzig, Georg Thieme, 1928.

[3] Four Centuries of Medical History in Canada, and a Sketch of the Medical History of Newfoundland. By John J. Heagerty, M.D., D.P.H. Univ. Chicago Press, 1928.

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THIS MONTH'S CONTRIBUTORS

ANOPOL, GEORGE, M.D., F.A.C.S., N. Y.
Assoc. Orth. Surg., N. Y. Post-Graduate Med. School and Hosp.; Attend. Orth., Community, Pan American & Columbus Hosp.

AUSTIN, ROBERT C., M.D., F.A.C.S., Dayton, Ohio.

BAGG, HALSEY J., PH.D., N. Y.
Biol. Memorial Hosp.; Research Fellow in Biol., Huntington Fund for Cancer Research.

BANDLER, CLARENCE G., M.D., F.A.C.S., N. Y.
Prof. Urol., N. Y. Post-Graduate Med. School; Attend. Urol., N. Y. Post-Graduate Hosp.; Assoc. Urol., Columbia Univ. Coll. of Phys. & Surg.; Asst. Att. Urol., Presbyterian Hosp.; Cons. Surgeon, Home for Aged & Infirm, Yonkers, King's Park State Hosp.

BARRINGER, BENJAMIN S., M.D., F.A.C.S., N. Y.
Surg., Urol. Dept., Memorial Hosp.; Cons. Urol., Mary McClellan & Nyack Hosp.; Att. Urol., Fifth Avenue Hosp.

BARTLETT, WILLARD, M.D., F.A.C.S., St. Louis.
Asst. Prof. Surg., Washington Univ. Med. School; Surg., Missouri Baptist San.

BARTLETT, WILLARD, JR., M.D., St. Louis.

BISSELL, DOUGAL, M.D., F.A.C.S., N. Y.
Cons. Surg., Woman's Hosp.; Att. Gynec., Central Islip State Hosp.

BONGARDT, HENRY F., M.D., F.A.C.S., Balt.
Asst. Surg., Univ. Maryland School of Med. & Coll. of Phys. & Surg.; Asst. Surg., Mercy Hosp.

BOOTHBY, WALTER M., M.D., F.A.C.S., Rochester, Minn.
Head, Sec. on Metab., Mayo Clin.; Assoc. Prof. Med., Mayo Found., Grad. School, Univ. of Minn.

BUZZANCA, ROSS, M.S., Birmingham, Ala.
Instr. Path., Univ. of Alabama School of Med.

DEAN, ARCHIE L., JR., M.D., N. Y.
Assoc. Att. Surg., Memorial Hosp.; Assoc. Urol., Fifth Ave. Hosp.; Visit. Urol., Reconstruction Hosp.; Cons. Urol., Somerset Hosp.

FRADKIN, WILLIAM Z. M.D., Brooklyn.

GRAHAM, ALLEN, M.D., F.A.C.S., Cleveland.
Surg. Path., Cleveland Clinic Hosp.

GURD, FRASER B., M.D., F.A.C.S., Montreal.
Lect. Surg., McGill Univ. Med. School; Surg., West. Pavilion, & Assoc. Surg., Main Pavilion, Montreal Gen. Hosp.

HAINES, SAMUEL F., M.D., Rochester, Minn.
Assoc., Sect. of Med., Mayo Clin.; Inst. in Med., Mayo Found., Grad. School, Univ. of Minn.

HALPERIN, S. J., M.D., N. Y.
Res. Path., N. Y. Post-Graduate Med. School & Hosp.

HAYNE, JAMES A., M.D., Charleston, S. C.
Sec. & State Health Officer; Prof., Public Health Administ., South Carolina Med. Coll.

KOLISCHER, G., M.D., Chicago.
Sr. G.-U. Surg., Michael Reese & Mount Sinai Hosp.

LAROCHELLE, A. H., M.D., Springfield, Mass.
Surg., Springfield Infirmary.

LAROCHELLE, F. D., M.D., Springfield, Mass.
Surg., Springfield Infirmary.

LUGINBUHL, C. B., M.D., Des Moines, Ia.

MCCARTHY, JOSEPH F., M.D., F.A.C.S., N. Y.
Dir., Dept. Urol., N. Y. Post-Graduate Med. School & Hosp.

MCKESSON, E. I., M.D., Toledo.
Anes., Flower, Lucas Co., St. Vincent's, Toledo, & Women's & Children's Hosp.

PACK, GEORGE T., M.D., N. Y.
Fellow, Memorial Hosp.

QUAIN, ERIC P., M.D., F.A.C.S., Bismarck, N. D.
Surg. & Chief of Staff, Bismarck Evangelical Hosp.; Surg., St. Alexius Hosp.

QUINBY, WILLIAM C., M.D., F.A.C.S., Boston.
Clin. Prof. G.-U. Surg., Med. School, Harvard Univ.; Urol., Peter Bent Brigham Hosp.

RATHBUN, NATHANIEL P., M.D., F.A.C.S., Brooklyn.
Att. Urol., Brooklyn, Lutheran & Unity Hosp.

RAVICH, ABRAHAM, M.D., F.A.C.S., Brooklyn.
Att. Urol., Jewish Hosp. of Brooklyn; Assoc. Urol., United Israel-Zion Hosp.; Chief Urol., Hebrew Home & Hosp. for Aged.

RIDGELY, IRWIN O., M.D., F.A.C.S., Baltimore.
Asst. Surg., Univ. of Maryland School of Med. & College of Phys. & Surg.; Assoc. Surg., Mercy Hosp.

RYGH, E. A., M.D., Minneapolis.
Bessesen Clinic.

SEARLS, HENRY H., M.D., F.A.C.S., San Francisco.
Asst. Prof. Surg., Univ. of California Med. School; Vis. Surg., Univ. of California Hosp., Laguna Honda Home.

SHERRY, LEROY B., M.D., F.A.C.S., Pasadena.
Surg. Staff, Pasadena Hosp.; Attend. Surg. Staff, Los Angeles, Gen. Hosp.

SLOAN, E. T., M.D., Bloomington, Ill.
Sloan Clinic.

STEPITA, C. TRAVERS, M.D., N. Y.
Asst. Prof. Urol., N. Y. Post-Graduate Med. School & Hosp.

WAGNER, H. H., M.D., Dayton.

WERSHUB, LEONARD, M.D., N. Y.
Asst. Att. Urol., Flower & Broad Street Hosp.; Asst. Inst. Urol., N. Y. Homeopathic Med. College & Flower Hosp.

WILSON, RALPH R., M.D., F.A.C.S., Kansas City.
Inst. Gynec., Univ. of Kansas School of Med.; Att. Obst. & Gynec., Kansas City Gen., Trinity Lutheran, & St. Luke's Hosp.; O. P. Att. Gynec., Bell Memorial Hosp.

WOLF HEINRICH F., M.D., N. Y.
Chief, Dept. Phys. Ther., Mt. Sinai Hosp. & Disp.; Inst. to Grad. Stud., Columbia Univ., Mt. Sinai Hosp.

WYETH, GEORGE A., M.D., N. Y.